

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
30 January 2003 (30.01.2003)

PCT

(10) International Publication Number  
**WO 03/007788 A2**

(51) International Patent Classification<sup>7</sup>:

A61B

(74) Agent: COFFEY, William, R.; Barnes & Thornburg, 11  
South Meridian Street, Indianapolis, IN 46204 (US).

(21) International Application Number: PCT/US02/22363

(22) International Filing Date: 15 July 2002 (15.07.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/305,786 16 July 2001 (16.07.2001) US  
60/388,951 14 June 2002 (14.06.2002) US

(71) Applicant (for all designated States except US): DEPUY  
PRODUCTS, INC. [US/US]; 700 Orthopaedic Drive,  
Warsaw, IN 46581 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): SCHWARTZ, Her-  
bert, Eugene [US/US]; 11702 Pennat Run, Fort Wayne, IN  
46845 (US). MALAVIYA, Prasanna [IN/US]; 3610 Win-  
terfield Run, Fort Wayne, IN 46804 (US). SINGLA, Amit,  
Kumar [US/US]; 215 Cambridge Station Road, Louisville,  
KY 40223 (US). PELO, Mark, Joseph [US/US]; 14180 E  
400 S, Macy, IN 46951 (US). PLOUHAR, Pamela, Lynn  
[US/US]; 17411 Battles Road, South Bend, IN 46614 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,  
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG,  
SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,  
VN, YU, ZA, ZM, ZW.

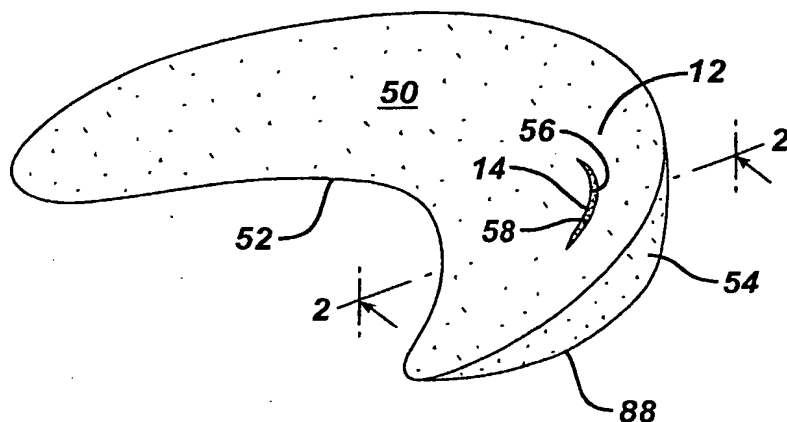
(84) Designated States (regional): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),  
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK,  
TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished  
upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: UNITARY SURGICAL DEVICE AND METHOD



(57) Abstract: Unitary surgical devices (10) are disclosed. One group of the illustrated devices has a pair of biocompatible, bioresorbable anchors (16, 18) connected to fixed lengths suture. The anchors (16, 18) and fixed length of suture are connected to each other prior to surgery. Another group of unitary surgical devices has a pair of fixating mechanisms (15, 17) connected to a base (21) prior to surgery. The second group of illustrated devices generally includes extracellular matrix material either as part of the base (21) or supported on the base (21). The extracellular matrix material serves as tissue regenerating material. In the second group of

unitary surgical devices, the fixating mechanisms illustrated generally comprise suture, anchors or pre-formed holes in the base. All of the illustrated unitary surgical devices are useful in repairing a damaged meniscus. The first group of unitary surgical devices can be used to approximate inner surfaces of a tear in the meniscus. The second group of devices can be used either as an insert to be placed between and approximated to the inner surfaces of the tear or as an insert to replace a void in the meniscus left after a meniscectomy.

WO 03/007788 A2

## UNITARY SURGICAL DEVICE AND METHOD

## CROSS REFERENCE TO RELATED APPLICATIONS

Cross reference is made to copending U.S. patent applications Serial  
5 No. XX/XXX,XXX entitled "Meniscus Regeneration Device and Method" (Attorney  
Docket No. 265280-71141, DEP-745); Serial No. XX/XXX,XXX entitled "Devices  
from Naturally Occurring Biologically Derived Materials" (Attorney Docket No.  
265280-71142, DEP-748); Serial No. XX/XXX,XXX entitled "Cartilage Repair  
Apparatus and Method" (Attorney Docket No. 265280-71143, DEP-749); Serial No.  
10 XX/XXX,XXX entitled "Hybrid Biologic/Synthetic Porous Extracellular Matrix  
Scaffolds" (Attorney Docket No. 265280-71144, DEP-751); Serial No.  
XX/XXX,XXX entitled "Cartilage Repair and Regeneration Device and Method"  
(Attorney Docket No. 265280-71145, DEP-752); Serial No. XX/XXX,XXX entitled  
"Porous Extracellular Matrix Scaffold and Method" (Attorney Docket No. 265280-  
15 71146, DEP-747); Serial No. XX/XXX,XXX entitled "Cartilage Repair and  
Regeneration Scaffolds and Method" (Attorney Docket No. 265280-71180, DEP-  
763); and Serial No. XX/XXX,XXX entitled "Porous Delivery Scaffold and Method"  
(Attorney Docket No. 265280-71207, DEP-762), each of which is assigned to the  
same assignee as the present application, each of which is filed concurrently herewith,  
20 and each of which is hereby incorporated by reference. Cross reference is also made  
to U.S. Patent Application Serial No. 10/172,347 entitled "Hybrid Biologic-Synthetic  
Bioabsorbable Scaffolds" which was filed on June 14, 2002, which is assigned to the  
same assignee as the present application, and which is hereby incorporated by  
reference.

25

## FIELD OF THE INVENTION

The present invention relates generally to surgical devices for  
approximating, repairing or regenerating damaged or diseased fibrocartilage, and to  
surgical methods using such devices.

## 30 BACKGROUND OF THE INVENTION

Articular cartilage is a type of hyaline cartilage that lines the surfaces  
of the opposing bones in a diarthrodial joint (e.g., knee, hip, shoulder, etc.). Articular

-2-

cartilage provides a near frictionless articulation between the bones, while also functioning to absorb and transmit the compressive and shear forces encountered in the joint. Further, since the tissue associated with articular cartilage is aneural, these load absorbing and transmitting functions occur in a painless fashion in a healthy joint.

Human joints also have another type of cartilage present: intra-articular fibrocartilage. Intra-articular fibrocartilage can be present in the form of a discus articularis, that is, as a plate or ring of fibrocartilage in the joint capsule separating the joint surfaces (articular cartilage) of the bones of the joint. Such fibrocartilage is present, for example, in the temporomandibular joint, between vertebrae, and in the knee joint. In the knee joint, the intra-articular fibrocartilage comprises the meniscus, a crescent-shaped or semi-lunar-shaped disc of tissue that is located between the femoral condyles and the tibial plateau. The meniscus primarily functions as a shock absorber, absorbing the shock of compressive and shear forces in the knee. The meniscus also provides a substantially frictionless surface for articulation of the knee joint.

When cartilage tissue is no longer healthy, there can be debilitating pain in the joint. Cartilage health can be adversely affected by disease, aging, or trauma. The adverse effects of disease, aging and trauma can be in the form of a tear in the cartilage or in the form of a breakdown of the cartilage matrix.

In the knee, the meniscus is frequently damaged in twisting injuries. It is also damaged with repetitive impact over time. Meniscus degeneration can also occur by aging; as a person ages, the meniscus can become soft in places, so that even common motions like squatting can cause meniscal tears.

Common surgical procedures for treating meniscal damage include tear repairs and menisectomies. A tear repair is most commonly performed when the tear is a clean longitudinal vertical lesion in the vascular red zone of the meniscus. The basic strategy is to stabilize the tear by limiting or eliminating radial separation of the faces of the tear when the meniscus is load bearing. Many devices and surgical procedures exist for repairing meniscal tears by approximating the faces of the meniscus at the tear. Examples of such devices and procedures are disclosed in the following U.S. Pats. Nos.: 6,319,271; 6,306,159; 6,306,156; 6,293,961; 6,156,044;

-3-

6,152,935; 6,056,778; 5,993,475; 5,980,524; 5,702,462; 5,569,252; 5,374,268;  
5,320,633; and 4,873,976.

Menisectomies involve the surgical removal of part of the meniscus. Such procedures have generally been performed in cases of radial tears, horizontal  
5 tears, vertical longitudinal tears outside the vascular zone, complex tears, or  
defibrillation. Although menisectomies provide immediate relief to the patient, in the  
long term the absence of part of the meniscus can cause cartilage wear on the  
condylar surface, eventually leading to arthritic conditions in the joint.

U.S. Pat. No. 6,042,610 assigned to ReGen Biologics, Inc., hereby  
10 incorporated by reference, discloses the use of a collagen scaffold device comprising  
a bioabsorbable material made at least in part from purified natural fibers. The  
purified natural fibers are cross-linked to form the device of that patent. The device  
produced can be used to provide augmentation for a damaged meniscus. Related U.S.  
Pat. Nos. 6,042,610; 5,735,903; 5,681,353; 5,306,311; 5,108,438; 5,007,934;  
15 4,880,429 also disclose a meniscal augmentation device for establishing a scaffold  
adapted for ingrowth of meniscal fibrochondrocytes.

It is also known to use naturally occurring extracellular matrices  
(ECMs) to provide a scaffold for tissue repair and regeneration. One such ECM is  
small intestine submucosa (SIS). SIS has been described as a natural biomaterial used  
20 to repair, support, and stabilize a wide variety of anatomical defects and traumatic  
injuries. See, for example, Cook® Online New Release provided by Cook Biotech  
Inc. at "www.cookgroup.com". The SIS material is derived from porcine small  
intestinal submucosa that models the qualities of its host when implanted in human  
soft tissues. Further, it is taught that the SIS material provides a natural matrix with a  
25 three-dimensional structure and biochemical composition that attracts host cells and  
supports tissue remodeling. SIS products, such as OASIS™ and SURGISIS™, are  
commercially available from Cook Biotech Inc., Bloomington, IN.

Another SIS product, RESTORE® Orthobiologic Implant, is available  
from DePuy Orthopaedics, Inc. in Warsaw, Indiana. The DePuy product is described  
30 for use during rotator cuff surgery, and is provided as a resorbable framework that  
allows the rotator cuff tendon to regenerate. The RESTORE Implant is derived from  
porcine small intestine submucosa, a naturally occurring ECM composed primarily of  
collagenous proteins, that has been cleaned, disinfected, and sterilized. Other

biological molecules, such as growth factors, glycosaminoglycans, etc., have also been identified in SIS. See: Hodde et al., *Tissue Eng.*, 2(3): 209-217 (1996); Voytik-Harbin et al., *J. Cell. Biochem.*, 67: 478-491 (1997); McPherson and Badylak, *Tissue Eng.*, 4(1): 75-83 (1998); Hodde et al., *Endothelium* 8(1): 11-24; Hodde and Hiles, 5 Wounds, 13(5): 195-201 (2001); Hurst and Bonner, *J. Biomater. Sci. Polym. Ed.*, 12(11): 1267-1279 (2001); Hodde et al., *Biomaterial*, 23(8): 1841-1848 (2002); and Hodde, *Tissue Eng.*, 8(2): 295-308 (2002). During seven years of preclinical testing in animals, there were no incidences of infection transmission from the implant to the host, and the RESTORE® Orthobiologic Implant has not adversely affected the 10 systemic activity of the immune system. See: Allman et al., *Transplant*, 17(11): 1631-1640 (2001); Allman et al., *Tissue Eng.*, 8(1):53-62 (2002).

While small intestine submucosa is available, other sources of submucosa are known to be effective for tissue remodeling. These sources include, but are not limited to, stomach, bladder, alimentary, respiratory, and genital 15 submucosa. In addition, liver basement membrane is known to be effective for tissue remodeling. See, e.g., U.S. Patents Nos. 6,379,710, 6,171,344, 6,099,567, and 5,554,389, hereby incorporated by reference. Further, while ECM is most often porcine derived, it is known that these various ECM materials can be derived from non-porcine sources, including bovine and ovine sources. Additionally, the ECM 20 material may also include partial layers of laminar muscularis mucosa, muscularis mucosa, lamina propria, stratum compactum layer and/or other such tissue materials depending upon other factors such as the source from which the ECM material was derived and the delamination procedure.

The following U.S. patents, hereby incorporated by reference, disclose 25 the use of ECMs for the regeneration and repair of various tissues: 6,379,710; 6,187,039; 6,176,880; 6,126,686; 6,099,567; 6,096,347; 5,997,575; 5,993,844; 5,968,096; 5,955,110; 5,922,028; 5,885,619; 5,788,625; 5,733,337; 5,762,966; 5,755,791; 5,753,267; 5,711,969; 5,645,860; 5,641,518; 5,554,389; 5,516,533; 5,460,962; 5,445,833; 5,372,821; 5,352,463; 5,281,422; and 5,275,826.

-5-

## SUMMARY OF THE INVENTION

The present invention is directed toward devices and surgical methods for the repair and regeneration of diseased or damaged intra-articular fibrocartilage such as the meniscus in the human knee joint.

5           In one aspect, the present invention provides a unitary surgical device for implantation in a patient for repairing a body tissue in the patient. The unitary surgical device comprises first and second biocompatible anchors and biocompatible tissue repair material extending between and connected to the first and second anchors. The anchors and tissue repair material are connected to each other prior to  
10 surgery. The first anchor includes at least one of the following: a bioresorbable barbed dart; a bioresorbable tack; a bioresorbable backstop; and a bioresorbable male locking member. The second anchor includes at least one of the following: a bioresorbable barbed dart; a bioresorbable tack; a bioresorbable backstop; and a bioresorbable female locking member. The biocompatible tissue repair material  
15 includes at least one of the following: a fixed length of suture; a sheet of collagen-containing material; laminar ECM material; formed ECM material; comminuted ECM material; ECM fibers; ECM foam material; a sheet of bioresorbable material; and a base connected to the first anchor and to the second anchor and a different material secured to the base, at least one of the base and the different material including ECM  
20 material.

          In another aspect, the present invention provides a unitary surgical device for surgical implantation in a patient for regenerating intra-articular fibrocartilage tissue in the patient. The unitary surgical device comprises a first  
25 fixating mechanism, a second fixating mechanism and tissue repair material extending between and connected to the first and second fixating members prior to surgery. The first fixating mechanism includes at least one of the following: a length of suture; a bioresorbable barbed dart; a bioresorbable tack; a bioresorbable backstop; and a bioresorbable male locking member. The second fixating mechanism includes at least one of the following: a length of suture; a bioresorbable barbed dart; a bioresorbable  
30 tack; a bioresorbable backstop; and a bioresorbable female locking member. The tissue repair material includes at least one of the following: a sheet of ECM material connected to the first anchor and the second anchor; laminar ECM material connected to the first anchor and the second anchor; ECM foam; comminuted ECM; ECM

-6-

fibers; cross-linked ECM material; formed ECM material; and a bioresorbable base connected to the first anchor and the second anchor and a different material on the base, where at least one of the base and the different material includes ECM.

5 In another aspect, the present invention provides a unitary surgical device for surgical implantation in a patient for regenerating intra-articular fibrocartilage tissue in the patient. The unitary surgical device comprises a base having at least two layers and a length of suture disposed or positioned between the layers of the base. At least part of the unitary surgical device is made from ECM material.

10 In another aspect, the present invention provides a unitary surgical device for surgical implantation in a patient for regenerating meniscal tissue in the patient. The unitary surgical device comprises a base having two panels. The two panels have a V-shaped configuration in cross-section, and meet along an apex portion. The two panels have end portions spaced distally from the apex portion. The two end portions are spaced from each other to provide a gap. The unitary surgical device may also include tissue regeneration material between the two panels of the base. The unitary surgical device also includes opposing anchors on the end portions of the base panels. The opposing anchors are suitable for fixation to the native meniscus.

15 In another aspect, the present invention provides a unitary surgical device for surgical implantation in a patient for regenerating tissue in the patient. The unitary surgical device comprises a base made of a bioresorbable polymer and ECM material on the base. In addition, the unitary surgical device includes a first fixating member secured to the base prior to surgery. The first fixating member is suitable for fixation to the patient's tissue.

20 In another aspect, the present invention provides a unitary surgical device for surgical implantation in a patient for regenerating tissue in the patient. The unitary surgical device comprises a base made of ECM material and a first fixating member secured to the base prior to surgery. The first fixating member is suitable for fixation to the patient's tissue.

25 In another aspect, the present invention provides a unitary surgical device for surgical implantation in a patient for regenerating tissue in the patient. The unitary surgical device comprises a base having two opposing edges and a plurality of

-7-

holes along one of the edges of the base. The unitary surgical devices includes ECM material.

In another aspect, the present invention provides a method of repairing a tear in the meniscus in the knee of a patient. The meniscus has an articulating surface and a non-articulating surface. The tear results in the meniscus having two inner surfaces. The method comprises the acts of providing a unitary surgical device having a pair of resorbable anchors and a fixed length of suture connected to the anchors. After the tear in the meniscus is located, the unitary surgical device is implanted to approximate the two inner surfaces of the meniscus at the tear, with suture extending across the articulating surface of the meniscus across the tear and the resorbable anchors being spaced from the tear.

In another aspect, the present invention provides a method of repairing a damaged meniscus in the knee of a patient. The meniscus has a non-articulating surface, a peripheral rim and an inner portion. The method comprises the acts of providing a wedge-shaped unitary surgical device including a fixating mechanism. A portion of the damaged meniscus inward of the peripheral rim of the meniscus is removed. The unitary surgical device is implanted with a portion inward of the peripheral rim. The unitary surgical device is fixated to the meniscus by fixating at least part of the base of the unitary surgical device to the meniscus with the fixating mechanism.

#### BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be better understood by reference to the figures of the drawings wherein like numbers denote like parts throughout and wherein:

FIG. 1 is a diagrammatic perspective view of a meniscus with a tear;  
FIG. 2 is a cross-section taken along line 2-2 of the meniscus of FIG. 1;

FIG. 3 is a perspective view of a first embodiment of a unitary surgical device of the present invention;

FIG. 4 is a cross-section of a torn meniscus showing the unitary surgical device of FIG. 3 fixated to the meniscus;

FIG. 5 is a perspective view of a second embodiment of a unitary surgical device of the present invention;



-8-

FIG. 6 is a cross-section of a torn meniscus showing the unitary surgical device of FIG. 5 fixated to the meniscus;

FIG. 7 is a perspective view of a third embodiment of a unitary surgical device of the present invention;

5           FIG. 8 is a cross-section of a torn meniscus showing the unitary surgical device of FIG. 7 fixated to the meniscus;

FIG. 9 is a perspective view of a fourth embodiment of a unitary surgical device of the present invention;

10           FIG. 10 is a cross-section of a torn meniscus showing the unitary surgical device of FIG. 9 fixated to the meniscus;

FIG. 11 is an elevation of a fifth embodiment of a unitary surgical device of the present invention;

15           FIG. 12 is a cross-section of a meniscus, after a partial menisectomy, showing the unitary surgical device of FIG. 11 fixated to the meniscus and at least partially filling the void left by the partial menisectomy;

FIG. 13 is a top plan view of a sixth embodiment of a unitary surgical device of the present invention;

FIG. 14 is an elevation of the unitary surgical device of FIG. 13;

20           FIG. 15 is a perspective diagrammatic view of a meniscus, with a void left by a partial menisectomy and with the unitary surgical device of FIGS. 13-14 in the process of being implanted;

FIG. 16 is a perspective diagrammatic view of the meniscus of FIG. 15, shown with the unitary surgical device of FIGS. 13-15 fixated to the meniscus;

25           FIG. 17 is a cross-section of the meniscus and unitary surgical device of FIG. 16, taken along line 17-17 of FIG. 16;

FIG. 18 is a top plan view of a seventh embodiment of a unitary surgical device incorporating the teachings of the present invention;

30           FIG. 19 is a cross-section of a meniscus, after a partial menisectomy, showing the unitary surgical device of FIG. 18 fixated to the meniscus and at least partially filling the void left by the partial menisectomy;

FIG. 20 is an elevation of an eighth embodiment of a unitary surgical device incorporating the teachings of the present invention;

FIG. 21 is a cross-section of a meniscus, after a partial menisectomy, showing the unitary surgical device of FIG. 20 fixated to the meniscus and at least partially filling the void left by the partial menisectomy;

FIG. 22 is a top plan view of a ninth embodiment of a unitary surgical  
5 device incorporating the teachings of the present invention;

FIG. 23 is a perspective view of the unitary surgical device of FIG. 22, shown with the top panel of the base folded over the mass of tissue regeneration material;

FIG. 24 is a perspective diagrammatic view of a meniscus, with a void  
10 left by a partial menisectomy;

FIG. 25 is a perspective diagrammatic view of a meniscus, with a void left by a partial menisectomy and with the unitary surgical device of FIGS. 22-23 in the process of being implanted;

FIG. 26 is a cross-section of a meniscus, after a partial menisectomy,  
15 showing the unitary surgical device of FIGS. 22-23 and 25 fixated to the meniscus and at least partially filling the void left by the partial menisectomy;

FIG. 27 is a top plan view of a tenth embodiment of a unitary surgical device incorporating the teachings of the present invention;

FIG. 28 is a bottom plan view of an eleventh embodiment of a unitary  
20 surgical device incorporating the teachings of the present invention;

FIG. 29 is a perspective, partially cut-away view of a meniscus with the unitary surgical device of FIG. 27 fixated to the meniscus;

FIG. 29A is a bottom plan view of a twelfth embodiment of a unitary surgical device incorporating the teachings of the present invention;

25 FIG. 29B is a side elevation of the embodiment of FIG. 29A;

FIG. 30 is a perspective view of a thirteenth embodiment of a unitary surgical device incorporating the teachings of the present invention;

FIG. 31 is a cross-section of a meniscus, after a partial  
30 menisectomy, showing the unitary surgical device of FIG. 30 fixated to the meniscus and at least partially filling the void left by the partial menisectomy;

FIG. 32 is an elevation of a fourteenth embodiment of a unitary surgical device incorporating the teachings of the present invention;

-10-

FIG. 33 is a cross-section of a meniscus, after a partial menisectomy, showing the unitary surgical device of FIG. 32 fixated to the meniscus and at least partially filling the void left by the partial menisectomy;

FIG. 34 is a perspective view of a fifteenth embodiment of a unitary surgical device incorporating the teachings of the present invention;

FIG. 35 is an elevation of a sixteenth embodiment of a unitary surgical device incorporating the teachings of the present invention;

FIG. 36 is a cross-section of a meniscus, after a partial menisectomy, showing the unitary surgical device of FIG. 35 fixated to the meniscus and at least partially filling the void left by the partial menisectomy;

FIG. 37 is an elevation of a seventeenth embodiment of a unitary surgical device incorporating the teachings of the present invention;

FIG. 38 is a cross-section of a meniscus, after a partial menisectomy, showing the unitary surgical device of FIG. 37 fixated to the meniscus and at least partially filling the void left by the partial menisectomy;

FIG. 39 is an elevation of an eighteenth embodiment of a unitary surgical device incorporating the teachings of the present invention;

FIG. 40 is a cross-section of a meniscus, after a partial menisectomy, showing the unitary surgical device of FIG. 39 fixated to the meniscus and at least partially filling the void left by the partial menisectomy;

FIG. 41 is an enlarged cross-section through a part of a laminar base of a unitary surgical device, such as the device of FIG. 35, with an implanted tack used as one of the anchors of the device;

FIG. 42 is a perspective view of a nineteenth embodiment of a unitary surgical device incorporating the teachings of the present invention;

FIG. 43 is an enlarged plan view of a mesh used as the base of a unitary surgical device;

FIG. 44 is a top plan view of a twentieth embodiment of a unitary surgical device incorporating the teachings of the present invention;

FIG. 45 is a top plan view of a twenty-first embodiment of a unitary surgical device incorporating the teachings of the present invention;

-11-

FIG. 46 is a cross-section through a torn meniscus, showing the unitary surgical device of FIG. 44 in place within the meniscal tear prior to approximation of the tissue;

5 FIG. 47 is a cross-section through a torn meniscus, showing the unitary surgical device of FIG. 45 in place within the meniscal tear prior to approximation of the tissue;

FIG. 48 is a cross-section through a torn meniscus, showing the unitary surgical device of FIGS. 44 and 47 in place within the meniscal tear after approximation of the meniscal tissue;

10 FIG. 49 is a cross-section through a torn meniscus, showing the unitary surgical device of FIGS. 45 and 48 in place within the meniscal tear after approximation of the meniscal tissue;

FIG. 50 is a perspective view of a twenty-second embodiment of the unitary surgical device of the present invention;

15 FIG. 51 is a perspective view of a portion of a meniscus, showing the unitary surgical device of FIG. 50 in use in repairing a tear in the meniscus;

FIG. 52 is a cross-section of a meniscus, after a partial menisectomy, showing the unitary surgical device of FIG. 37 fixated to the meniscus and at least partially filling the void left by the partial menisectomy; and

20 FIG. 53 is a perspective view of a twenty-third embodiment of the unitary surgical device of the present invention, in place on a meniscus.

#### DETAILED DESCRIPTION OF THE ILLUSTRATED EMBODIMENTS

A variety of unitary surgical devices 10 utilizing the principles of the present invention are illustrated in the accompanying drawings. The illustrated  
25 surgical devices 10 are for implantation in a patient for repairing a body tissue in the patient. The illustrated embodiments would most commonly be used in repairing intra-articular fibrocartilage, such as the meniscus of the knee, although the invention is not so limited unless expressly called for in the claims. A meniscus, or part of a meniscus, is diagrammatically illustrated at 12 in the accompanying drawings (FIGS.  
30 1-2, 4, 6, 8, 10, 12, 15-17, 19, 21, 24-26, 29, 31, 33, 36, 38, 40, 46-49, 51 and 52). An example of a meniscal tear is shown at 14 in FIGS. 1-2, 4, 6, 8, 10, 46, 47 and 51.

-12-

The invention is also expected to be useful in the treatment of damaged and diseased intra-articular fibrocartilage in other body parts as well.

As used herein "unitary" refers to the fact that the surgical devices 10 include at least one fixating element 15 and at least one tissue repair element 20, as an integral unit, prior to the time that the surgical devices are implanted in the patient. Preferably, each unitary surgical device 10 also includes a second fixating element 17. Thus, for example, suture may be incorporated into the device prior to the time the device is implanted in the patient. However, it should be understood that although at least one of each element is included in the device, the surgeon may choose to use additional material during surgery. For example, the surgeon may opt during surgery to use an additional fixating mechanism that was not an integral part of the original device, if the surgeon believes that additional stabilization is necessary or desirable.

As used herein, "tissue repair element" and "tissue repair material" are intended to include materials such as suture, whether of natural or synthetic origin, as well as tissue or cartilage regeneration material. Tissue or cartilage regeneration material encompasses naturally occurring extracellular matrix (ECM) materials that provide a collagen scaffold for tissue repair and regeneration. One such ECM material that may be used for the tissue or cartilage regeneration material is submucosa, and small intestine submucosa (SIS) in particular. Other bioremodelable collagenous tissue matrices, whatever the source, are intended to be included within "tissue regeneration material", including purified collagenous tissues. As used herein, "SIS" is intended to include small intestine submucosa unless otherwise limited. Moreover, as used herein, "ECM" is intended to include all SIS, as well as materials made from the other sources of submucosa identified above (e.g., bladder, stomach and liver tissue from bovine, ovine and porcine sources) and materials derived from liver basement membrane (from whatever source) unless otherwise limited. For the purposes of this invention, it is within the definition of a naturally occurring ECM to clean, delaminate, and/or comminute the ECM, to cross-link the collagen within the ECM, and to form a foam or other structure from the ECM. It is also within the definition of naturally occurring ECM to fully or partially remove one or more components or subcomponents of the naturally occurring matrix. However, it is not within the definition of a naturally occurring ECM to extract or separate and purify the natural components or subcomponents (e.g., collagen or growth factor) and reform

-13-

a matrix material from these extracted and purified components or subcomponents. Also, while reference is made to SIS, it is understood that other naturally occurring ECMs such as stomach, bladder, alimentary, respiratory, and genital submucosa, and liver basement membrane, for example, whatever the source (e.g., bovine, porcine, ovine, etc.) are within the scope of this invention. Thus, in this application, the terms “naturally occurring extracellular matrix” or “naturally occurring ECM” are intended to refer to extracellular matrix material that has been cleaned, disinfected, sterilized, and optionally cross-linked. The terms “naturally occurring ECM” and “naturally occurring extracellular matrix” are also intended to include foam material made from naturally occurring ECM as described in copending U.S. Patent Application Serial No. XX/XXX,XXX entitled “Porous Extracellular Matrix Scaffold and Method” (Attorney Docket No. 265280-71146, DEP-747), the toughened material made from naturally occurring ECM as described in U.S. Patent Application Serial No. XX/XXX,XXX entitled “Meniscus Regeneration Device and Method” (Attorney Docket No. 265280-71141, DEP-745), and the hardened material made from naturally occurring ECM as described in U.S. Patent Application Serial No. XX/XXX,XXX entitled “Devices from Naturally Occurring Biologically Derived Materials” (Attorney Docket No. 265280-71142, DEP-748), all filed concurrently herewith as U.S. Provisional Patent Applications and incorporated by reference below.

As used herein, bioresorbable, resorbable and bioabsorbable are intended to be interchangeable. All three terms are intended to mean materials that are naturally degradable *in vivo* over time. All are intended to include both natural and man-made materials, and to include new materials as they are developed, unless a specific material or type of material is identified in the claims.

As used herein, “intra-articular fibrocartilage” is intended to include the meniscus in the knee joint. It is also intended to include fibrocartilage separating the joint surfaces (articular cartilage) of the bones of other joints and separating the surfaces of adjacent vertebrae. “Intra-articular fibrocartilage” thus includes, for example, fibrocartilage in the temporomandibular joint and between vertebrae.

Although the embodiments of the invention illustrated in FIGS. 11-23, 25-42, 44-47 and 53 are shaped for use in the meniscus, it should be understood that the principles of the present invention may be applied to surgical devices to be used in repairing and

-14-

regenerating damaged or diseased intra-articular fibrocartilage in other joints in the body.

ECM material, and combinations of ECM material and synthetic materials, for use in the present invention can be prepared as described in the following United States Patents, utility applications for United States patents, and provisional applications for United States Patents, the disclosures of which are incorporated by reference herein: U.S. Pat. No. 4,902,508, entitled "Tissue Graft Composition"; U.S. Pat. No. 4,956,178, entitled "Tissue Graft Composition"; U.S. Pat. No. 5,281,422, entitled "Graft for Promoting Autogenous Tissue Growth"; U.S. Pat. No. 5,372,821, entitled "Graft for Promoting Autogenous Tissue Growth"; U.S. Pat. No. 5,445,833, entitled "Tendon or Ligament Graft for Promoting Autogenous Tissue Growth"; U.S. Pat. No. 5,733,337, entitled "Tissue Repair Fabric"; U.S. Pat. No. 5,788,625, entitled "Method of Making Reconstructive SIS Structure for Cartilaginous Elements In Situ"; U.S. Pat. No. 5,922,028, entitled "Multi-layered SIS Tissue Graft Construct for Replacement of Cartilaginous Elements In Situ"; U.S. Pat. No. 5,955,110, entitled "Multilayered Submucosal Graft Constructs and Method for Making the Same"; U.S. Pat. No. 5,993,844, entitled "Chemical Treatment, Without Detergents or Enzymes, of Tissue to Form an Acellular collagenous Matrix"; U.S. Pat. No. 6,176,880, entitled "Tissue Graft Construct for Replacement of Cartilaginous Structures"; U.S. Pat. App. Ser. No. 09/918,116, filed July 30, 2001, entitled "Reinforced Small Intestine Submucosa"; U.S. Pat. App. Serial No. 09/767,345, filed January 23, 2001, entitled "Tissue Graft Construct for Replacement of Cartilaginous Structures"; U.S. Pat. App. Ser. No. 09/767,346, filed January 23, 2001, entitled "Tissue Graft Construct for Replacement of Cartilaginous Structures"; U.S. Provisional Application Serial Number 60/305,786, entitled "Meniscus Regeneration Device and Method", filed on July 16, 2001.

The "ECM" for use in the present invention can be disinfected as described in U.S. Patent No. 6,206,931, entitled "Graft Prosthesis Materials" or U.S. Pat. No. 5,460,962, entitled "Peracetic Acid Sterilization of Collagen or collagenous Tissue," which are incorporated by reference herein in their entireties, or may be disinfected generally through the use of a disinfecting agent such as a 0.15% peracetic acid in 20% ethanol solution.

-15-

As described above, ECM material as used herein includes commercially available materials, unless otherwise expressly limited. Such commercially available materials include those available from DePuy Orthopaedics, Inc. of Warsaw, Indiana (e.g., RESTORE® Orthobiologic Implant), for example.

5                   It should also be understood that "ECM" materials, including "SIS", as used herein, are not limited to the materials or processes described in the preceding paragraphs unless expressly indicated otherwise; the patents, provisional applications, utility applications and commercial products identified in the preceding paragraphs are identified for purposes of illustration only.

10                   Referring now to the illustrated embodiments of the present invention, one group of unitary surgical devices 10 is illustrated in FIGS. 3-10 and 50-52. As illustrated in FIGS. 3, 5, 7, 9 and 50, each unitary surgical device 10 of this group includes two fixating elements 15, 17: a first anchor 16 and a second anchor 18. Each unitary surgical device also includes tissue repair material 20 extending between and  
15                   connected to the first anchor 16 and second anchor 18. The tissue repair material 20 is connected to the two fixating members 15, 17 prior to surgery, and prior to terminal sterilization of the unitary surgical devices. In this group, the tissue repair material 20 comprises suture. A second group of unitary surgical devices 10 is illustrated in  
20                   FIGS. 11-23, 25-40, 42 and 44-49. As illustrated in FIGS. 11, 13, 15, 18, 20, 22, 23, 27, 28, 30, 34, 35, 37, 39, 44, 45 and 50, each illustrated unitary surgical device 10 of this group also includes two fixating elements 15, 17 and tissue repair material 20 extending between and connected to the fixating members 15, 17. In this second group, the tissue repair material 20 includes a tissue regeneration material 22; the tissue repair material 20 may also include other elements such as suture or a base 21.  
25                   In addition, in this second group, although the fixating elements 15, 17 may include anchors 16, 18, the fixating elements may also include suture, either alone or in combination with the anchors 16, 18. Thus, the fixating members 15, 17 may comprise: one or more anchors 16, 18; one or more anchors 16, 18 combined with suture 16g, 18g; or suture 16g, 18g alone. All of these elements in the second group  
30                   are secured together prior to surgery and prior to terminal sterilization of the unitary surgical devices.

                  In both groups of devices, where at least one of the fixating members 15, 17 includes an anchor, the anchor 16 may comprise: a barbed dart, as illustrated at



-16-

16a in FIGS. 3-4, 7-8, 9-10, 30-34 and 50-52; a tack, as illustrated at 16b in FIGS. 35-36; a backstop, as illustrated at 16c in FIGS. 5-6; a male locking member, as illustrated at 16d in FIGS. 37-40; or a pair of connected anchors such as the pair of barbed darts 16a connected by a length of suture. The first fixating member 15 may also comprise a length of suture, as shown at 16g in FIGS. 11-15, 17-23, 25-26, 28-29, 42 and 44. The first fixating member 15 may also comprise combinations of anchors and other materials, such as a combination of a barbed dart 16a as an anchor and a length of suture 16g, as shown in FIGS. 30-31 and 46-47, or a combination of a male locking member 16d and a length of suture 16g, as shown in FIGS. 39-40, for example. Whatever form of fixating member is selected, each material in the illustrated embodiments is a biocompatible and bioabsorbable one, that is, one that will eventually be broken down, assimilated, diminished or excreted, or both assimilated and diminished or excreted by the body of the patient. If a second fixating member 17 is used, it may include a second anchor 18. The second anchor 18 may comprise a top hat-shaped fixating member, as illustrated at 18a in FIGS. 3-4; a backstop, as illustrated at 18b in FIGS. 5-8; barbed dart, as illustrated at 18c in FIGS. 9-10, 27, 30-31 and 50-51; a receiving opening, as shown at 18d in FIG. 34; a tack, as illustrated at 18e in FIGS. 35-36; a female locking member, as illustrated at 18f in FIGS. 37-40. The second fixating member 17 may also comprise a length of suture, as shown at 18g in FIGS. 13-23, 25-26, 28-29, 42 and 44-45. The second fixating member 17 may also comprise combinations of materials, such as a combination of an anchor 18 such as a barbed dart 18c and a length of suture 18g, as shown in FIGS. 30-31 and 46-47, for example. As in the case of the first fixating member 15, whatever structure or form is selected for the second fixating member 17, each material in the illustrated embodiments is a biocompatible and bioabsorbable one.

In unitary surgical devices 10 using two fixating members 15, 17, various combinations of the above-described anchors 16a-16g, 18a-18g can be used. For example, two anchors may be used of the same or different shape, such as: a barbed dart 16a with a top hat-shaped structure 18a, as shown in FIGS. 3-4; a barbed dart 16a with another barbed dart as shown at 16a and 18c in FIGS. 9-10; a barbed dart with a backstop, as shown at 16a and 18b in FIGS. 7-8; a tack 16b can be used with another tack 18e, as shown in FIGS. 35-36, or with some other structure. All of these combinations may be used with suture as the tissue repair material 20 in the first

-17-

group of embodiments, and all of them may be used with the second group of embodiments as well. It should be understood that these combinations are identified for purposes of illustration only. The present invention is not limited to these combinations unless expressly set forth in the claims.

5                   A variety of materials may be used for the first and second anchors 16, 18. For example, the anchors may be constructed of biocompatible polymers, bioremodelable collagenous matrices and combinations of such materials. Other materials, such as bioactive agents, other biologically derived agents, biocompatible inorganic materials, cells, and biological lubricants can also be included as part of the  
10   anchors.

                  As used herein, "biocompatible polymer" and "biocompatible polymers" is intended to include both synthetic polymers and biopolymers (e.g., collagen). Examples of biocompatible polymers include: polyesters of [alpha]-hydroxycarboxylic acids, such as poly(L-lactide) (PLLA) and polyglycolide (PGA);  
15   poly-p-dioxanone (PDS); polycaprolactone (PCL); polyvinyl alcohol (PVA); polyethylene oxide (PEO); polymers disclosed in United States Pat. Nos. 6,333,029 and 6,355,699; and any other bioresorbable and biocompatible polymer, co-polymer or mixture of polymers or co-polymers that are utilized in the construction of prosthetic implants. If other such polymers have therapeutic value in the orthopaedic  
20   field, it is anticipated that at least some of them will have use in the present invention, and at least some of them should be included in "biocompatible polymers." In addition, as new biocompatible, bioresorbable materials are developed, it is expected that at least some of them will be useful materials from which the anchors may be made. It should be understood that the above materials are identified by way of  
25   example only, and the present invention is not limited to any particular material unless expressly called for in the claims.

                  "Bioremodelable collagenous tissue matrix" and "naturally occurring bioremodelable collagenous tissue matrix" are intended to include matrices derived from native tissue selected from the group comprising skin, artery, vein, pericardium,  
30   heart valve, dura mater, ligament, bone, cartilage, bladder, liver, stomach, fascia and intestine, whatever the source. Although "naturally occurring bioremodelable collagenous tissue matrix" is intended to refer to matrix material that has been cleaned, processed, sterilized, and optionally cross-linked, it is not within the

-18-

definition of a naturally occurring bioremodelable collagenous tissue matrix to extract and purify the natural components or subcomponents (e.g., collagen) and reform or reconstitute a matrix material from purified natural components or subcomponents.

It is understood and intended that there is substantial overlap between  
5 “bioremodelable collagenous tissue matrices” and “extracellular matrices”; the different expressions are used in this specification and claims to ensure complete coverage of the invention. It is believed that the teachings of the present invention will be useful for materials falling with both definitions.

Some commercially available products may be used as the anchors 16,  
10 18 in some of the illustrated embodiments. For example, the backstop elements shown at 16c, 18b and 19 in FIGS. 5-8, 45, 47 and 50-52 and top-hat-shaped element 18a shown in FIGS. 3-4 may be taken from the RAPIDLOC™ Meniscal Repair System available from the MITEK® Products division of ETHICON, INC. of Westwood, Massachusetts.

15 In addition, the anchors 16a-16f, 18a-18f may be constructed from a naturally occurring material such as naturally occurring extracellular matrices (ECM), such as small intestine submucosa (SIS). In such a case, each anchor 16a-16f, 18a-18f may be configured as a monolithic structure formed from naturally occurring ECM which is cured to be rigid and hardened. As such, it should be appreciated that  
20 the ECM material from which the anchor is fabricated is cured to produce a structure that possesses the necessary hardness and toughness to be inserted into and through the native meniscus and to be retained in the native meniscus for at least a predetermined period of time.

ECM material with the necessary hardness and toughness for use as the  
25 anchors may be fabricated by compacting comminuted or shredded naturally occurring ECM material into bar or rod stock by compressing the material together and then curing the material such that it is very rigid and hardened. The curing may be accomplished by simple air drying or by heated air drying of the formed stock. The material may additionally be cross-linked to further improve its mechanical  
30 properties.

As a specific example, one or more of the anchors 16a-16f, 18a-18f may be constructed with a cured and hardened SIS. In this case, comminuted SIS material is placed in a container and allowed to air dry for a predetermined period of

-19-

time (e.g., as long as several days) at room temperature. Over such a time, water evaporates from the SIS material thereby shrinking the material. The shrunk material is very tough and hard and, as a result, may be machined as described herein.

It should be appreciated that other process parameters may be established to facilitate the curing process. For example, a curing profile utilizing predetermined amounts of heat and/or pressure may be designed to facilitate the curing of the naturally occurring ECM material (e.g., SIS).

Once the ECM material (e.g., SIS) is cured to a desired hardness and toughness, it may be machined with conventional machining equipment to desired shapes such as in the shape of a barbed dart as illustrated in FIGS. 3-4, 7-10, 27, 30-33 and 46-47. For example, the anchor 16a-16f, 18a-18f may be turned on a lathe or similar equipment to produce the desired configuration of the anchor, such as the barbed darts. However, based on the specific design of the anchor, it should be appreciated that certain features of the anchor (e.g., the barbed darts) may be separately or additionally machined to produce a desired shape or geometry. For example, various barb configurations may be formed on part of the anchor, by, for example, use of a cutting machine.

In addition to conventional cutting machining techniques (e.g., lathing and cutting), contemporary techniques may also be utilized to form the cured naturally occurring ECM into the desired configuration of the anchor 16a-16f, 18a-18f. For example, a programmable laser cutting machine may be used to cut the raw stock of cured ECM. Specifically, the laser cutting machine may be programmed to cut the raw stock in a pattern which produces a desired configuration of the anchor. In addition to providing for cutting with precision tolerances, laser cutting also provides other benefits. Such laser cutting of the ECM can produce barbed darts having cut edges which are sealed and fused together to enhance the attachment capability of the barbed darts.

It should be understood that the material selected for the anchors 16a-16f, 18a-18f may also comprise mixtures or composites of the materials described above. For example, the anchors 16a-16f, 18a-18f could comprise both a biocompatible polymer and ECM material. With regard to the shape of the barbed darts 16a, 18c that may be used with the present invention, reference is made to barbed dart configuration shown in U.S. Pat. No. 5,702,463 as one example of a shape

-20-

of barbed dart that may be useful. It should be understood that the shapes of the barbed darts 16a, 18c and other anchors 16b-16f, 18a-18b, 18d-18f shown in the accompanying drawings are provided for purposes of illustration only. The present invention is not limited to any particular shape of barbed dart or other anchor unless expressly set forth in the claims. It should also be understood that the sizes of the anchors in the drawings shown are provided for purposes of illustration only. The actual sizes of the anchors may be different from those illustrated, and may vary with the method used to implant them. For example, the commercially available backstop is inserted through a needle, as shown in the Mitek Products document "RAPIDLOC  
5 MENISCAL REPAIR SYSTEM, Surgical Technique for Repair of Meniscal Tears". If this technique and instrumentation is to be used to insert the anchors of the present invention, then the anchors should be sized accordingly. Typical barbed darts can be expected to be in the range of about 1 mm in maximum diameter and about 3 mm in length. It should be understood that these dimensions are provided for purposes of  
10 illustration only; the present invention is not limited to any particular size of anchor unless expressly set forth in the claims.

Where the fixating elements 15, 17 include or consist of suture 16g, 18g, such as in FIGS. 11-23, 25-31, 42 and 44, any suitable suture material may be used, such as commercially available suture. Acceptable suture may be obtained from  
20 the MITEK PRODUCTS division of ETHICON, INC. of Westwood, Massachusetts; examples include PANACRYL™ absorbable suture, ETHIBOND® EXCEL polyester suture, PDS® polydioxanone suture and PROLENE® polypropylene suture.

Whatever structure and material is chosen for the anchors 16, 18, the anchors are connected to a tissue repair material 20 in the illustrated unitary surgical  
25 devices 10. The tissue repair material 20 in the illustrated embodiments includes: suture; a base; tissue regenerating material; or combinations of these materials.

In the embodiments of FIGS. 3-10, the tissue repair material 20 comprises a fixed length of suture; the suture in the illustrated embodiment has a length of about 4-5 mm. A surgical kit could contain several unitary surgical devices  
30 10, each with a pair of anchors 16, 18 separated by a variety of fixed lengths of suture 20 as the tissue repair material. The lengths for the sutures portions of the devices 10 in the kit could range, for example, from 2 mm to about 1 cm. Alternatively, several kits could be provided each with a plurality of unitary surgical devices of a particular

-21-

length. It should be understood that these lengths are provided for purposes of illustration only; the present invention is not limited to tissue repair material of these or any particular lengths unless expressly called for in the claims. The suture used for the tissue repair material 20 in these embodiments may be standard commercially available suture made of conventional materials. Acceptable suture may be obtained from the sources identified above. FIGS. 3-10 illustrate examples of such unitary surgical devices 10 wherein the tissue repair material 20 comprises suture.

Embodiments of the invention utilizing a base 21 as part of the tissue repair material 20 are illustrated in FIGS. 11-23, 25-42, 44-47. The base component 21 of the tissue repair material may comprise a third fixating member, such as backstop element 19 shown in FIG. 50. In addition, the base 21 may provide structural support to the unitary surgical device 10. The base may comprise a sheet, as shown in FIGS. 11-23, 25-42, and 44-45, and may be a laminar sheet, as illustrated in FIG. 41. The base component may comprise a formed structure, as illustrated in FIG. 42. The formed structures could be laminar or could be formed in other manners as disclosed below. The base component 21 may also comprise one or more layers of mesh structures, for example, woven materials as illustrated in FIG. 43, non-woven materials, knitted materials, warp-knitted materials, braided materials, foamed materials and combinations of those materials; if more than one layer of a mesh structure is provided, the layers may be juxtaposed or spaced, with other material sandwiched between the layers, for example. The base material should have sufficient strength so that the connection to the anchors 16, 18 and the connection of the anchors 16, 18 to the patient's native tissue is maintained during implantation of the unitary surgical device 10 and for a suitable period of time after implantation. Generally, the base 21 should have sufficient strength for a sufficient time to allow the healing process to progress to the point where the structural stability provided by the base 21 is no longer needed. However, in the claims no particular strength should be implied the claims unless expressly recited.

The base 21 in any of the embodiments of FIGS. 11-23, 25-42, 44-47 could comprise a biocompatible polymer, a bioremodelable collagenous matrix, a naturally occurring ECM (and in particular SIS) or combinations of these materials. The tissue regeneration material 22 may be carried by the base 21 or may comprise the base 21. The base could also comprise these materials together with bioactive

-22-

agents, other biologically derived agents, cells, a biological lubricant, or a biocompatible inorganic material. In the claims, no particular material or combination of materials should be implied for the base unless expressly recited.

For a base 21 made out of or including a biocompatible polymer, suitable polymers are defined above. These polymers can be provided in the form of, for example, meshes of woven or non-woven materials, laminar sheets, knitted materials, warp-knitted materials, braided materials, or one or more layers of foamed polymer. Reference is also made to the materials disclosed in copending U.S. Serial No. XX/XXX,XXX entitled "Hybrid Biologic/Synthetic Porous Extracellular Matrix Scaffolds" (Attorney Docket No. 265280-71144, DEP-751), filed concurrently herewith, along with U.S. Patent Application Serial No. 10/172,347 entitled "Hybrid Biologic-Synthetic Bioabsorbable Scaffolds" which was filed on June 14, 2002, both of which are incorporated by reference herein in their entireties.

For a base 21 made out of or including ECM material, several options are available. The ECM could comprise material derived from a mammalian submucosa source, such as SIS. The ECM base could be formed as a laminate structure, as illustrated in FIG. 41. The layers may be laminated together and bonded by both mechanical compression and application of vacuum and/or heated air which accomplishes the bonding and also dries the product. Reference is made to U.S. Patent No. 5,955,110, which is incorporated by reference herein in its entirety, for a description of a method of making layered SIS material. A suitable SIS base may also be formed as described in copending U.S. Patent Application Serial No. XX/XXX,XXX entitled "Meniscus Regeneration Device and Method" (Attorney Docket No. 265280-71141, DEP-745), which is incorporated by reference herein in its entireties. A vacuum plate or platen with a cavity in a desired shape may be provided, with a vacuum pump connected to the cavity by a tube. The cavity may be provided with a plurality of openings leading to a manifold space within the platen which is connected to the pump. Several layers of naturally occurring ECM, such as SIS, are placed on the plate. These layers are preferably initially in a moist and flexible state. These moist, flexible layers are pulled down into the cavity by the vacuum to form a molded recess for receiving a mass of biological material. A flat vacuum plate or platen could also be used to form flat sheet forms of ECM material.

-23-

These and other techniques may be employed to form the base into a desired shape, such as the wedge shape shown in FIGS. 11-23, 25-26 and 30-40.

Other sheet forms of ECM are expected to be useful to provide a base 21 or combination base 21 and tissue regeneration material 22. For example, it is anticipated that one could make a thick slurry of comminuted ECM fibers, dry the slurry into a sheet, pocket or other form, such as the form illustrated in FIG. 42, for example, and heat the material under combinations of pressure, vacuum and heat to bond and dry the product. In addition, one or more such sheets could be laminated together or with strips of ECM material. It is expected that other shapes and forms could also be formed of such materials. It is expected that other materials could be intermixed with the ECM material as well; for example, the thick slurry could include both ECM material and a biocompatible polymer as a structural reinforcement, or the slurry of ECM material could be supported on and fused with a supporting structure made of ECM or some biocompatible polymer.

In any of the above examples, the material for the base, such as ECM, can be cross-linked by known methods. For example, chemical or physical cross-linking can be used. Chemical cross-linking methods include the use of aldehydes, carbodiimides, glycation agents, enzymes or the like. Physical cross-linking methods include freeze-drying and fusion by physical means such as heat (thermal cross-linking), radiation (ultraviolet or gamma irradiation) or combinations such as by drying at elevated temperatures (dehydrothermal cross-linking). Cross-linking may also be used to impart to the base 21 biological lubricants such as hyaluronic acid (HA).

A portion or all of the base 21 may be perforated to allow easy chemical and cellular transfer. In addition, if desired, cells, bioactive agents, biologically derived agents, biological lubricants and biocompatible inorganic materials may be added to the base.

The base 21 may also include a foamed or hybrid structure, and may include other materials as disclosed in applications for United States Patent filed concurrently herewith and previously filed, which are incorporated by reference herein in their entireties: U.S. Patent Application Serial No. 10/172,347 entitled "Hybrid Biologic-Synthetic Bioabsorbable Scaffolds" which was filed on June 14, 2002; Serial No. XX/XXX,XXX entitled "Hybrid Biologic/Synthetic Porous



-24-

Extracellular Matrix Scaffolds” (Attorney Docket No. 265280-71144, DEP-751) filed herewith; Serial No. XX/XXX,XXX entitled “Cartilage Repair and Regeneration Device and Method” (Attorney Docket No. 265280-71145, DEP-752) filed herewith; and Serial No. XX/XXX,XXX entitled “Porous Extracellular Matrix Scaffold and Method” (Attorney Docket No. 265280-71146, DEP-747) filed herewith.

The base 21 may take any one of several shapes and configurations. For example, as illustrated in FIGS. 27-29, the base 21 may comprise a single substantially flat panel. As illustrated in FIGS. 10-23, 25-26 and 30-40, the base 21 may comprise two integral panels 24, 26 joined along a linear or curved apex 28; the two illustrated panels 24, 25 diverge outward from the apex 28 to define a wedge-shaped or V-shaped structure in cross-section. The side edges 30, 32 of each panel 24, 26 may also diverge outwardly from the apex 28, as shown in FIGS. 13, 18, 22-23 and 30. The base 21 may comprise a pillow-like structure, like a sac made of the base material, with a mass of tissue regeneration material held within the sac or pillow structure.

In each of the embodiments of FIGS. 11-23, 25-40, 42 and 44-45, a mass of tissue regeneration material 22, such as ECM, is included as part of the tissue repair material 20. In each of these embodiments, the mass of tissue regeneration material 22 comprises a separate mass that is secured to the base 21. In the embodiment of FIG. 44, a plurality (three) of masses of tissue regeneration material 22 are fixed to the base 21. In the embodiments of FIGS. 11-23, 25-26 and 30-40, a single mass of tissue regeneration material 22 is positioned between the two panels 24, 26 near the apex 28; the masses of tissue regeneration material 22 in these illustrated embodiments are wedge-shaped or V-shaped in cross-section, although it should be understood that other shapes are within the scope of the invention. As illustrated in FIG. 42, the mass of tissue regeneration material could also comprise a loose pack of comminuted or shredded ECM material. As disclosed in United States Provisional Patent Application Serial No. 60/305,786, the SIS material could comprise rolls of comminuted SIS. It should also be understood that, depending on the material used for the base 21, the unitary surgical device need not include any additional tissue regeneration material; for example, if the base 21 comprises one or more layers of ECM mesh or an ECM foam, then it may not be necessary to include a separate mass of tissue regeneration material.

-25-

If a separate mass of tissue regeneration material 22 is used, it may be secured to the base 21 by use of a compatible adhesive. Synthetic adhesives are commercially available, such as polycaprolactone (PCL). Biological adhesives are also available, such as commercially available materials containing transglutaminase or fibrin, for example. Other biological adhesives are also known, as described in U.S. Pat. No. 6,326,025 "Tissue Reactive Adhesive Compositions" and in published U.S. Pat. Apps. 200200344533 "Bioerodable Polymeric Adhesives for Tissue Repair" and 20020031551 "Bioerodable Polymeric Adhesives for Tissue Repair." The adhesive can be applied to the tissue regeneration material 22 and to the base 21. The tissue regeneration material 22 may be secured to a pillow or sac-like base by substantially enclosing the mass of tissue regeneration material within the base structure, such as by suturing three or four sides of the base structure around the mass of tissue regeneration material, by using a compatible adhesive around the perimeter of the base surrounding the mass of tissue regeneration material. The tissue regeneration material may also be secured to the base by positioning the tissue regeneration material in a formed receiving structure or pocket, as in the embodiment of FIG. 42. In addition, layers of SIS material could be laminated around all or part of the mass of tissue regeneration material. Chemical and physical cross-linking may also be used to secure the mass of tissue regeneration material 22 to the base 21. Chemical cross-linking methods of securing these materials 21, 22 together include the use of aldehydes, carbodiimides, glycation agents, enzymes (e.g., transglutaminase), biologins (e.g fibrin) or the like. Physical cross-linking methods include freeze-drying and fusion by physical means such as heat (thermal cross-linking), radiation (ultraviolet or gamma irradiation) or combinations such as by drying at elevated temperatures (dehydrothermal cross-linking).

The mass or plug of tissue regeneration material 22 may comprise comminuted and/or lyophilized naturally occurring ECM (e.g., SIS) with the desired porosity and material density. The material density and/or porosity of the mass or plug may be varied to control cell migration and proliferation. Additional examples of materials that are usable for the mass of tissue regeneration material include ECM (e.g., SIS) powder, ECM (e.g., SIS) fibers, ECM (e.g., SIS) threads, ECM (e.g., SIS) mesh, ECM (e.g., SIS) wovens, ECM (e.g., SIS) non-wovens, ECM (e.g., SIS) braided materials, ECM (e.g., SIS) solutions, ECM (e.g., SIS) gel, ECM (e.g., SIS)

-26-

paste, ECM (e.g., SIS) foam, and combinations of such materials. For the powder, solutions, gel and paste forms of SIS, the material may be prepared as described in U.S. Patent No. 5,352,463, entitled "Tissue Graft for Surgical Reconstruction of a Collagenous Meniscus and Method Therefor", which is incorporated by reference  
5 herein in its entirety. It should be understood that separate reference in the above list to the forms of ECM should not be taken to imply that the listed references are exclusive; for example, ECM non-wovens, ECM threads and ECM foam may all include ECM fibers.

The mass or plug of tissue regeneration material 22, and the base 21, or  
10 the combination of the base and the tissue regeneration material may include materials described in U.S. Patent No. 6,179,872 B1, entitled "Biopolymer Matt for Use in Tissue Repair and Reconstruction" and U.S. Patent No. 6,153,292, entitled "Biopolymer Foams for Use in Tissue Repair and Reconstruction", which are both incorporated by reference herein in their entireties. The mass or plug of tissue  
15 regeneration material 22 and the base, or the combination of the base and the tissue regeneration material may include materials disclosed in the following copending and concurrently filed U.S. patent applications, which are incorporated by reference herein: Serial No. XX/XXX,XXX entitled "Meniscus Regeneration Device and Method" (Attorney Docket No. 265280-71141, DEP-745); Serial No. XX/XXX,XXX  
20 entitled "Devices from Naturally Occurring Biologically Derived Materials" (Attorney Docket No. 265280-71142, DEP-748); Serial No. XX/XXX,XXX entitled "Cartilage Repair Apparatus and Method" (Attorney Docket No. 265280-71143, DEP-749); Serial No. XX/XXX,XXX entitled "Hybrid Biologic/Synthetic Porous Extracellular Matrix Scaffolds" (Attorney Docket No. 265280-71144, DEP-751);  
25 Serial No. XX/XXX,XXX entitled "Cartilage Repair and Regeneration Device and Method" (Attorney Docket No. 265280-71145, DEP-752); Serial No. XX/XXX,XXX entitled "Porous Extracellular Matrix Scaffold and Method" (Attorney Docket No. 265280-71146, DEP-747); Serial No. XX/XXX,XXX entitled "Cartilage Repair and Regeneration Scaffolds and Method" (Attorney Docket No. 265280-71180, DEP-  
30 763); and Serial No. XX/XXX,XXX entitled "Porous Delivery Scaffold and Method" (Attorney Docket No. 265280-71207, DEP-762), along with U.S. Patent Application Serial No. 10/172,347 entitled "Hybrid Biologic-Synthetic Bioabsorbable Scaffolds" which was filed on June 14, 2002.

-27-

The mass of plug of tissue regeneration material 22 could also comprise other collagenous materials. For example, it is expected that a commercial product such as the Collagen Meniscus Implant made by ReGen Biologics, Inc. of Franklin Lakes, New Jersey could be combined with other elements of the present invention to form a unitary surgical device. Other collagen scaffolds are described in the following U.S. Patents: 6,042,610; 5,735,903; 5,479,033; 5,306,311; 5,007,934; and 4,880,429.

Porous ECM (e.g., SIS) foam for the tissue regeneration material 22 may be fabricated by lyophilizing (i.e., freeze-drying) comminuted ECM (e.g., SIS) suspended in water. The material density and pore size of the resultant foam may be varied to fit the needs of the design by controlling, amongst other things, the rate of freezing of the comminuted ECM suspension and/or the amount of water in which the comminuted ECM is suspended at the on-set of the freezing process.

The following is a specific example of a process for fabricating an exemplary ECM foam. It should be understood that the present invention is not limited to the materials, devices, or process steps of the following example unless expressly called for in the claims. The first step in developing a foam with a desired pore size and density is the procurement of comminuted ECM. To do this, scissor-cut ECM runners (e.g., SIS runners about 6 inches long) are positioned in a 1700 series Comitrol™ machine which is commercially available from Urschel Laboratories of Valparaiso, Indiana. The ECM material is processed and thereafter collected in a receptacle at the output of the machine. The material is then processed through the machine a second time under similar conditions. Water is introduced during the process, and the resultant material is a "slurry" of ECM fiber (thin, long fibers about 200 microns thick x 1-5 mm long) suspended substantially uniformly in water. It should be understood that this size of ECM fiber is identified as an illustrative example only; the invention is not limited to a particular size of ECM fiber material unless the claims expressly call for a particular size.

Generally, the process parameters for the comminution process should be selected to produce ECM material that is capable of commingling, intermixing or intertwining, rather than producing a powder. Process parameters that can be varied using the above-identified 1700 series Comitrol™ machine include the choice of blade used, whether water is used, the amount of water used, the speed at which the

-28-

blades turn and the number of times the material is passed through the machine. As an example, cutting head 140084-10 and a Vericut, sealed impeller from Urschel Laboratories may be used, with a flow of water of about two (2) gallons per minute, with the cutting head run at a constant speed of about 9300 rpm. A first pass through the machine at these parameters will produce fibrous ECM material of varying sizes, and a second pass will produce ECM fibers of more uniform size. To test the comminuted material to determine whether it is appropriate for the production of an ECM foam, the comminuted ECM suspension or slurry is then centrifuged, excess water is poured off and the remaining slurry is poured into a dish. By hand, a small amount of the comminuted ECM material in the dish is pinched between the thumb and index finger and gently lifted from the dish; if the comminuted SIS material is fibrous, at least a small amount of additional ECM, beyond the portion pinched between the thumb and index finger, will lift along with the material that has been pinched. This additional comminuted ECM material lifts with the material that is between the thumb and index finger because the individual pieces of comminuted ECM material are commingled or intertwined. Such material should be suitable for the production of a foam. It is expected that other shapes and sizes of ECM material, and mixtures of shapes and sizes of ECM material, may be useful in producing an ECM foam. For example, it is expected that one could comminute ECM to produce ECM flakes that can intermingle to form an appropriate slurry.

As used herein, unless the claims are otherwise expressly limited, the terms "cohesive ECM pieces" and "cohesive SIS pieces" are intended to include ECM and SIS material that has been comminuted or otherwise processed to produce ECM and SIS pieces that are capable of commingling or intertwining (in the wet or dry state) to form a cohesive mass of discrete elements, regardless of the shape or shapes of the individual ECM or SIS pieces. One method of demonstrating that the ECM material comprises cohesive pieces is the "pinch test" described above. Examination of the final ECM foam product produced may also provide evidence that the base material comprised cohesive ECM pieces.

As used herein, "pieces" is intended to include any fiber, strip, ribbon, sliver, filament, shred, bit, fragment, part, flake, slice, cut, chunk, or other portion of solid or solid-like material. "ECM fiber" and "SIS fiber" are also intended to include ECM and SIS material that has been comminuted or otherwise processed to produce a

-29-

material wherein at least some of the individual pieces of ECM and SIS material have lengths greater than their widths and thicknesses. It should be understood that unless otherwise expressly limited by the claims, use of the terms "ECM pieces" and "SIS pieces" should be construed to mean that the material includes such pieces, but should not be considered to imply that the material consists of such pieces exclusively. Such terms should also not be construed to imply that any particular process has been used to produce the material.

After the suspension has been formed, the suspension of SIS fibers is dried. To do so, a lyophilization process (freeze drying) is used. In particular, the suspension of SIS fibers is frozen at a controlled temperature drop rate to control the size of the formed ice crystals. Without allowing the material to thaw, the process of lyophilization sublimates ice crystals directly to vapor under vacuum and low temperatures. This process leaves voids in the spaces previously occupied by ice crystals. These voids and the SIS fibrous material form a network of compartments with SIS material defining interconnected walls of the network compartments. One exemplary machine for performing such a freeze drying process is a Virtis Genesis™ Series lyophilizer which is commercially available from SP Industries, Inc. of Gardiner, New York.

The process parameters of the lyophilization process may be varied to produce foams of varying pore sizes and material densities. For example, to produce foams having a relatively small pore size and a relative high material density, the SIS fibrous material may be tightly compacted by removing the water in a substantially uniform manner so as to achieve a relatively high density. Thereafter, the SIS fibrous material is flash-frozen using liquid nitrogen prior to lyophilization of the SIS. To produce foams having a moderate pore size and a moderate material density, the SIS fibrous material is first tightly compacted by removing the water in a substantially uniform matter so as to achieve a relatively high density. Thereafter, the SIS is frozen at a relatively fast rate (e.g.,  $>-1^{\circ}\text{C}/\text{min.}$ ) to a temperature of about  $-80^{\circ}\text{C}$  prior to lyophilization of the SIS.

As shown in the photomicrographs (FIGS. 1-3) in co-pending U.S. Patent Application Serial No. XX/XXX,XXX entitled "Porous Extracellular Matrix Scaffold and Method" (Attorney Docket No. 265280-71146, DEP-747), filed by Prasanna Malaviya, Herbert Schwartz and Pamela Plouhar, the result of using the

-30-

above-described process and materials is an ECM foam comprising a three-dimensional web of naturally occurring ECM defining a plurality of three-dimensional pores. The foam has three-dimensional pores throughout its height, width and thickness; the three-dimensional pores are interconnected to define a plurality of interconnected passageways. These interconnected passageways may be used for movement of cells such as chondrocytes *in vivo*. These interconnected passageways can also be used for the introduction of bioactive agents, biologically derived agents (e.g., stimulants), cells, biocompatible inorganic materials, biocompatible polymers and/or biological lubricants that may be combined with the foam as described below prior to implantation. The interconnected passageways defined by the three-dimensional pores also serve as passageways for materials used during the manufacturing process, such as compounds used for chemical cross-linking the foam.

The tissue regeneration material 22 may be chemically cross-linked with, for example, aldehydes, carbodiimides, glycation agents, enzymes (e.g., transglutaminase), biologins (e.g., fibrin) or the like. The tissue regeneration material 22 may also be physically cross-linked, by, for example: freeze-drying, heat fusion (thermal cross-linking), radiation fusion (ultraviolet or gamma irradiation) or combinations of fusion techniques such as by drying at elevated temperatures (dehydrothermal cross-linking).

The base 21 and/or the mass of tissue regeneration material 22 may also be impregnated with bioactive agents, biologically derived agents, cells, biocompatible polymers, biocompatible inorganic materials and biological lubricants. The materials could be cross-linked or otherwise affixed to the ECM base and/or mass. Alternatively, cells (e.g., fibrochondrocytes) may be cultured on the ECM base and/or mass, and as a result, subsequently be implanted as part of the unitary surgical device at the time of implantation. For the meniscus repair device, any such cells are preferably fibrochondrocytes or mesenchymal stem cells.

"Bioactive agents" include one or more of the following: chemotactic agents; therapeutic agents (e.g., antibiotics, steroidal and non-steroidal analgesics and anti-inflammatories, anti-rejection agents such as immunosuppressants and anti-cancer drugs); various proteins (e.g., short chain peptides, bone morphogenic proteins, glycoprotein and lipoprotein); cell attachment mediators; biologically active ligands;

integrin binding sequence; ligands; various growth and/or differentiation agents (e.g., epidermal growth factor, IGF-I, IGF-II, TGF- $\beta$  I-III, growth and differentiation factors, vascular endothelial growth factors, fibroblast growth factors, platelet derived growth factors, insulin derived growth factor and transforming growth factors, parathyroid hormone, parathyroid hormone related peptide, bFGF; TGF $\beta$  superfamily factors; BMP-2; BMP-4; BMP-6; BMP-12; sonic hedgehog; GDF5; GDF6; GDF8; PDGF); small molecules that affect the upregulation of specific growth factors; tenascin-C; hyaluronic acid; chondroitin sulfate; fibronectin; decorin; thromboelastin; thrombin-derived peptides; heparin-binding domains; heparin; heparan sulfate; DNA fragments and DNA plasmids . If other such substances have therapeutic value in the orthopaedic field, it is anticipated that at least some of these substances will have use in the present invention, and such substances should be included in the meaning of "bioactive agent" and "bioactive agents" unless expressly limited otherwise. It should be understood that the above agents are identified by way of example only, and the present invention is not limited to any particular agent unless expressly called for in the claims.

"Biologically derived agents" include one or more of the following: bone (autograft, allograft, and xenograft) and derivatives of bone; cartilage (autograft, allograft and xenograft), including, for example, meniscal tissue, and derivatives; ligament (autograft, allograft and xenograft) and derivatives; derivatives of intestinal tissue (autograft, allograft and xenograft), including for example submucosa; derivatives of stomach tissue (autograft, allograft and xenograft), including for example submucosa; derivatives of bladder tissue (autograft, allograft and xenograft), including for example submucosa; derivatives of alimentary tissue (autograft, allograft and xenograft), including for example submucosa; derivatives of respiratory tissue (autograft, allograft and xenograft), including for example submucosa; derivatives of genital tissue (autograft, allograft and xenograft), including for example submucosa; derivatives of liver tissue (autograft, allograft and xenograft), including for example liver basement membrane; derivatives of skin (autograft, allograft and xenograft); platelet rich plasma (PRP), platelet poor plasma, bone marrow aspirate, demineralized bone matrix, insulin derived growth factor, whole blood, fibrin and blood clot. Purified ECM and other collagen sources are also intended to be included within "biologically derived agents." If other such substances have therapeutic value



-32-

in the orthopaedic field, it is anticipated that at least some of these substances will have use in the present invention, and such substances should be included in the meaning of "biologically derived agent" and "biologically derived agents" unless expressly limited otherwise. It should be understood that the above agents are  
5 identified by way of example only, and the present invention is not limited to any particular agent unless expressly called for in the claims.

"Cells" include one or more of the following: chondrocytes; fibrochondrocytes; osteocytes; osteoblasts; osteoclasts; synoviocytes; bone marrow cells; mesenchymal cells; stromal cells; stem cells; embryonic stem cells; precursor  
10 cells derived from adipose tissue; peripheral blood progenitor cells; stem cells isolated from adult tissue; genetically transformed cells; a combination of chondrocytes and other cells; a combination of osteocytes and other cells; a combination of synoviocytes and other cells; a combination of bone marrow cells and other cells; a combination of mesenchymal cells and other cells; a combination of stromal cells and  
15 other cells; a combination of stem cells and other cells; a combination of embryonic stem cells and other cells; a combination of precursor cells isolated from adult tissue and other cells; a combination of peripheral blood progenitor cells and other cells; a combination of stem cells isolated from adult tissue and other cells; and a combination of genetically transformed cells and other cells. If other cells are found  
20 to have therapeutic value in the orthopaedic field, it is anticipated that at least some of these cells will have use in the present invention, and such cells should be included within the meaning of "cell" and "cells" unless expressly limited otherwise. It should be understood that the above cells are identified by way of example only, and the present invention is not limited to any particular type of cell unless expressly called  
25 for in the claims.

"Biological lubricants" include: hyaluronic acid and its salts, such as sodium hyaluronate; glycosaminoglycans such as dermatan sulfate, heparan sulfate, chondroitin sulfate and keratan sulfate; synovial fluid and components of synovial fluid, including mucinous glycoproteins (e.g., lubricin), tribonectins, articular  
30 cartilage superficial zone proteins, surface-active phospholipids, lubricating glycoproteins I, II; vitronectin; and rooster comb hyaluronate. "Biological lubricant" is also intended to include commercial products such as ARTHREASE<sup>TM</sup> high molecular weight sodium hyaluronate, available in Europe from DePuy International,

-33-

Ltd. of Leeds, England, and manufactured by Bio-Technology General (Israel) Ltd., of Rehovot, Israel; SYNVISCO® Hylan G-F 20, manufactured by Biomatrix, Inc., of Ridgefield, New Jersey and distributed by Wyeth-Ayerst Pharmaceuticals of Philadelphia, Pennsylvania; HYLAGAN® sodium hyaluronate, available from  
5 Sanofi-Synthelabo, Inc., of New York, New York, manufactured by FIDIA S.p.A., of Padua, Italy; and HEALON® sodium hyaluronate, available from Pharmacia Corporation of Peapack, New Jersey in concentrations of 1%, 1.4% and 2.3% (for ophthalmologic uses). If other such substances have therapeutic value in the orthopaedic field, it is anticipated that at least some of these substances will have use  
10 in the present invention, and such substances should be included in the meaning of "biological lubricant" and "biological lubricants" unless expressly limited otherwise. In addition, as new biological lubricants are identified or developed, it is expected that at least some of them will be useful materials for the present invention. It should be understood that the above materials are identified by way of example only, and the  
15 present invention is not limited to any particular material unless expressly called for in the claims.

"Biocompatible inorganic materials" include materials such as hydroxyapatite, all calcium phosphates, alpha-tricalcium phosphate, beta-tricalcium phosphate, calcium carbonate, barium carbonate, calcium sulfate, barium sulfate,  
20 polymorphs of calcium phosphates, ceramic particles and combinations of such materials. If other such substances have therapeutic value in the orthopaedic field, it is anticipated that at least some of these substances will have use in the present invention, and such substances should be included in the meaning of "biocompatible inorganic material" and "biocompatible inorganic materials" unless expressly limited  
25 otherwise.

It is expected that various combinations of bioactive agents, biologically derived agents, cells, biological lubricants, biocompatible inorganic materials, biocompatible polymers can be used with the anchors, bases, and tissue repair material (including tissue regeneration material) of the present invention.

30 The unitary surgical devices 10 of FIGS. 11-23, 27-40 and 42 may be sized to fit the standard gap 70 left in the meniscus by a menisectomy so that one unitary surgical device can be implanted to fill this gap 70. It may be desirable to make a plurality of sizes of such unitary surgical devices 10 to encompass the

-34-

standard range of gaps 70 left by menisectomies. In addition, it may be desirable to plan to be able to use more than one unitary surgical device 10 to fill the gap 70 left by the menisectomy, so that a plurality of unitary surgical devices 10 may be implanted adjacent to or overlapping with one another to fill the gap 70 during the surgery.

To make a unitary surgical device 10 that includes two anchors 16, 18 connected by a length of suture as the tissue repair material 20, the anchors may be formed as described above. The anchors 16a-16g, 18a-18g may be formed to include, or machined to include an opening so that one end of each length of suture may be secured to one anchor. For example, the anchors 16, 18 could be tubular so that one end of suture can be threaded through each anchor and then knotted to secure them together. Or, the anchors could have a hole through which the suture end is threaded and then knotted.

To make a unitary surgical device 10 that includes both a laminar base and suture, as in the embodiments of FIGS. 22-23, 25-26 and 30-31, threads of suture 34 may be placed between two layers of base material prior to completely forming the base so that the suture threads 34 become integral with the base 21 during the forming process. As illustrated, the lengths of the suture threads 34 should be great enough so that the suture ends extend substantially beyond the parallel end edges 36, 38 of the unitary surgical device to define the first fixating element 15 and second fixating element 17 at the opposite ends of the suture thread 34. As illustrated, a plurality of suture threads may be made integral with each base. In the embodiments of FIGS. 22-23 and 30-31, three long strands of suture 34 are used, so that the resulting unitary surgical device has a total of six fixating elements: the first fixating element 15, the second fixating element 17, a third fixating element 40, a fourth fixating element 42, a fifth fixating element 44, and a sixth fixating element 46. The three suture threads 34 for this embodiment may be aligned so that one length of suture is positioned along the longitudinal centerline of the base, and additional lengths of suture are positioned between the longitudinally aligned thread and the long edges 30, 32 of the base 21, and aligned with the shape of the long edges 30, 32 of the base 21. The laminar base 21 may then be made as described in the provisional application with each suture thread 34 in place between two layers. The finished unitary surgical device 10 will include the suture affixed to the base. The base 21 of FIG. 22 may then be folded

-35-

about axis 48 to form the wedge-shaped structure shown in FIG. 23, with the linear apex 28 at the axis 48. If desired, additional anchors such as barbs, tacks, or backstops, for example, could be secured to the free ends of the suture, as illustrated in the embodiment of FIGS. 30-31. It should be understood that fewer or more strands of suture may be used for the devices illustrated in FIGS. 22-23 and 30-31; for example, two strands of suture could be used, or four strands of suture could be used.

For non-laminar bases, the suture threads 34 could be positioned in or on the base material prior to final forming of the base. The base may then be formed as described above with the suture formed as an integral part of the base. In any case, suture could also be adhered to the base or could be sewn to the base.

To make the embodiments of FIGS. 34-38, an anchor such as a barb may be positioned on the surface of base laminates, as shown in FIG. 41, where anchor 16b is shown on layers 23i-23l of laminate. Then, additional layers, such as layers 23a-23h shown in FIG. 41, may be placed on the initial base laminate 23i-23l, surrounding part of the anchor 16b. The unitary surgical device may then be formed with the anchor 16b becoming secured to at least some of the layers of the base as the layers are dried, heated and compressed. Other forms of anchor can be positioned on the base during fabrication of the base so that completion of the base also secures the anchors to the base to form a unitary structure.

Any of the anchors could also be secured to the base after the base is formed by, for example, using an adhesive to secure the anchor to the base. Suitable adhesives for this purpose include commercially available materials such as those containing fibrin or transglutaminase. It should be understood that other methods for securing the anchors to the base are within the scope of this invention; the invention is not limited to any particular method of securing the elements together unless expressly called for in the claims.

All of the illustrated embodiments of the invention may be prepared for use in surgery by providing prepackaged unitary surgical devices or kits. Thus, for example, after making any of the illustrated embodiments of unitary surgical device, a single unitary surgical device can be packaged and terminally sterilized, so that the surgeon may simply open the package and implant the device. It may be desirable to prepackage a kit including several unitary surgical devices of different sizes. As discussed above, for the embodiments of FIGS. 3-10, a kit could include

-36-

several unitary surgical devices 10, each with a pair of anchors 16, 18 separated by a variety of fixed lengths of suture 20 as the tissue repair material. For the embodiments of FIGS. 11-23, 25-40, 42 and 44-45, 53, each device could be made in a plurality of sizes, such as small, medium and large; a kit could comprise a group of unitary surgical devices of all sizes or a group of unitary surgical devices all of one size, for example. Conventional commercially available packaging materials and sterilization techniques can be used. For example, gamma irradiation or electron beam irradiation can be used for this terminal sterilization. It should be understood however, that the present invention is not limited to any particular packaging material or sterilization technique unless expressly called for in the claims.

If any of the embodiments are to be seeded with living cells such as chondrocytes, the terminally sterilized implant can subsequently be seeded with living cells and packaged in an appropriate medium for the cell type used. For example, a cell culture medium comprising Dulbecco's Modified Eagles Medium (DMEM) can be used with standard additives such as non-essential amino acids, glucose, ascorbic acid, sodium pyruvate, fungicides, antibiotics, etc., in concentrations deemed appropriate for cell type, shipping conditions, etc.

Use of the illustrated embodiments of the invention is described below. All of the embodiments of the present invention may be used in surgical repair of a damaged meniscus 12, as illustrated in FIGS. 1-2, where the meniscal injury is illustrated as a meniscal tear 14 extending down from the top bearing surface 50 of the meniscus 12 between the inner arcuate edge 52 of the meniscus 12 and the back or outer arcuate surface 54 of the meniscus 12. It should be understood that the drawings show the meniscus 12 in simplified form for purposes of illustration only.

The first group of illustrated unitary surgical repair devices, illustrated in FIGS. 4-10, are useful for surgical meniscal repairs. With each of these devices, the objective is the same: to position the anchors 16, 18 beyond the tear 14, and to position the tissue repair material 20, comprising suture in the embodiments of FIGS. 4-10, across the tear 14. For each of these embodiments, a surgical kit would generally be provided with several unitary surgical devices 10, with varying lengths of suture, provided in the kit. The meniscal tear is evaluated and the meniscus is prepared in the standard manner. From the initial evaluation, the surgeon determines the length of device that is needed to extend across the meniscal injury for the

-37-

particular patient, and then selects one of the devices from the surgical kit. Using the embodiments illustrated in FIGS. 4 and 8, at least one of the anchors, such as first anchor 16, is positioned within the meniscus 12, while the second anchor 18 is positioned on the back arcuate surface 54 of the meniscus, with the suture 20

5 connecting the anchors and extending across the tear 14. The first anchor 16 is pushed far enough into the meniscus to approximate the two inner surfaces 56, 58 of the meniscal tear 14. The shapes of the anchors 16, 18 hold their final position. Neither anchor is exposed on a bearing surface of the meniscus. For the embodiments of FIGS. 4 and 8, preferably the anchor 18 that bears against the back non-bearing

10 surface 54 of the meniscus is positioned first, and then the anchor 16 that extends into the interior of the meniscus is positioned. A tubular needle such as that used with the RAPIDLOC<sup>TM</sup> Meniscal Repair System could be employed. Such a device could have a cable or similar structure running through the needle and connected to a trigger or similar device to selectively to implant one of the anchors. The surgeon could

15 insert the needle through the top articular surface 50 of the meniscus, and push the needle through the body of the meniscus until reaching the back surface 54. The trigger may then be operated to release one of the anchors, such as anchor 18 in FIG. 4, against the back surface 54 of the meniscus. At this stage, a length of suture 20 extends out of the top surface 50 of the meniscus and extends to the other anchor 16.

20 The surgeon may then use a pair of forceps of similar device and push the anchor 16 through the top surface 50 and into the body of the meniscus until the two surface 56, 58 at the tear are approximated. Both anchors 16, 18 should then stay in place, holding the meniscus as shown in FIG. 4 so that the meniscus can heal. Similar surgical procedures may be used to implant the embodiments of the unitary surgical

25 devices 10 illustrated in FIGS. 6 and 10. It should be understood that this surgical technique is provided by way of example only, and that the present invention is not limited to any particular surgical technique unless expressly called for in the claims. Additional unitary surgical devices 10 can be implanted until all the tissue surfaces are adequately approximated and the tear is stabilized.

30 In some instances, it may be desirable to facilitate healing of the torn meniscus by using a unitary surgical device 10 of the type shown in FIGS. 44 and 45. With these embodiments of the invention, the base 21 and tissue regeneration material 22 are thin, and nearly planar in cross section. The anchoring devices 16, 18 are used

-38-

for delivering the unitary surgical device to the proper location in the meniscal tear 14, between the two inner surfaces 54, 56 of the meniscal tear 14. With these devices, the first anchor 16, or first and second anchors 16, 18, are inserted on the end of one or two needles (not shown), and the needles are pushed through the inner surface 58 of the meniscal tear 14 and through the body of the meniscus and out through the back side 54 of the meniscus 12. The anchoring device or devices 16, 18 are moved through the back 54 of the meniscus until one of the faces 60 of the unitary surgical device 10 is juxtaposed with the inner surface 58 of the meniscal tear 14, as shown in FIGS. 46 and 47. The remaining suture at the back of the meniscus may be cut off, removed and discarded. Once the unitary surgical device 10 is in place in the meniscal tear 14 as shown in FIGS. 46-47, the surgeon may then approximate the meniscal inner surface 56 and the opposite face 62 of the base 21 of the unitary surgical device 10, and secure the parts in this position using suture or another unitary surgical device, such as one of the devices of FIGS. 4-10. FIGS. 48 and 49 illustrate the meniscus with the tear 14 approximated to the implanted unitary surgical device 10. In FIG. 48, the surfaces of the meniscus and the implanted unitary surgical device are secured together with suture, shown at 64, while in FIG. 49, the surfaces are secured together with another unitary surgical device 10 of the type shown in FIG. 4.

Instruments that may be used in delivering the unitary surgical devices of FIG. 45 may include a Meniscal Applier (REF 228000) available from the Mitek Products division of Ethicon, Inc., of Westwood, Massachusetts. The Mitek Meniscal Applier may be modified to provide a greater curvature if desired. 90° mosquito forceps may also be used to implant the unitary surgical devices.

If the injury or damage to the meniscus 12 is so severe that a menisectomy or partial menisectomy is necessary, the surgeon may remove a portion of the meniscus as illustrated in FIGS. 15 and 24. Generally, the surgeon will remove the damaged or diseased tissue, as shown in FIGS. 15 and 24, leaving a generally wedge-shaped void 70. It should be understood that the illustrations in FIGS. 15 and 24 are simplified for purposes of illustration; the actual area of removed tissue may look different from that illustrated. The portion of the meniscus that is removed is from the inner arcuate edge 52 of the meniscus to a position inward of the back arcuate surface 54 of the meniscus, so that an arcuate portion of the back 54 of the meniscus remains after the menisectomy. This back portion to the meniscus, shown

-39-

at 72 in FIGS. 15-17, 19, 21, 24-26, 29, 31, 33, 36, 38 and 40. Although the menisectomy can extend to the highly vascularized red zone of the meniscus, the back portion 72 can include more than red zone tissue.

With part of the meniscus 12 removed, the surgeon may opt to use one of the embodiments of the unitary surgical device 10 illustrated in FIGS. 11-23, 25-40 and 42. Considering each embodiment in order, the unitary surgical device 10 of the FIG. 11 embodiment is wedge shaped in cross-section, and may be placed so that the tissue regeneration material and the base 21 fit within the void 70 left after part of the meniscus has been removed. The first and second anchors 16, 18 comprise two lengths of suture secured to a disc 73 of biocompatible and bioabsorbable material. The first and second anchoring sutures extend through a part of the tissue regeneration material 22, and out through the lower face of the base 21. These anchoring sutures 16, 18 may be pushed through the back portion 72 of the meniscus as shown in FIG. 12, and pulled tight until the back surface 74 of the device 10 is juxtaposed with the front surface 76 of the back portion 72 of the meniscus. The ends of the two anchoring sutures 16, 18 may then be tied against the back surface 54 of the meniscus 12 as shown in FIG. 12.

In the embodiment of FIG. 13, the base 21 is somewhat larger than the wedge of tissue regeneration material 22, extending rearward of the back surface 74 of the tissue regeneration material 22 and forming upper and lower projections 80, 82 as shown in FIG. 14. In this embodiment, the first and second anchoring sutures 16, 18 comprise a length of suture extending substantially across one dimension of the base 21 at the back of the base, and out through holes 78 in the base 21. The two anchor sutures 16, 18 may be inserted with a needle or similar device (not shown) through the front surface 76 of the back red portion 72 of the meniscus, or through the bottom surface of the body of the meniscus. The two anchoring sutures 16, 18 may be pushed through the body of the meniscus and through the arcuate back surface 54, where they may be tied off, as shown in FIG. 17. As shown in FIGS. 16-17, the unitary surgical device substantially fills the void 70 left by the menisectomy. As shown in FIG. 17, the front surface 76 of the vascularized portion 72 of the meniscus abuts the back surface 74 of the tissue regeneration material 22 so that the blood vessels may deliver cells and other materials to the tissue regeneration material 22 for the healing process.



-40-

The anchoring sutures 16, 18 may also be along the top of the base 21, as shown in the embodiment of FIGS. 18-19, and the upper projection 80 may be greater than the lower projection 82. It should be understood that the lower projection could also be made to be greater than the upper projection 80.

5 As shown in FIGS. 20-21, the anchoring sutures 16, 18 can also be connected directly to the back surface 74 of the mass of tissue regeneration material 22. To make such a unitary surgical device 10, these anchoring sutures 16, 18 could be positioned prior to final forming of the tissue regeneration material, adhered to the tissue regeneration material or mechanically attached to the tissue regeneration  
10 material, such as by sewing the suture to the tissue regeneration material; any of these methods of securing the anchors 16, 18 to the tissue regeneration material 22 would be performed prior to implantation of the unitary surgical device. Also as shown in FIG. 20, the top portion of the base 21 need not be secured to the mass of tissue regeneration material 22, the top portion of the base 21 could instead be sutured to the  
15 back vascularized portion 72 of the meniscus, as shown at 86 in FIG. 21.

As shown in the embodiment of FIGS. 22-23, 25 and 26, a plurality of anchors 16, 18, 40, 42, 44, 46 may be provided. As shown in FIGS. 25-26, the unitary surgical device 10 of FIGS. 22-23 may be implanted by extending one group of sutures 16, 40, 44 over the top of the vascularized portion 72 of the meniscus, one  
20 group of sutures 18, 42, 46 under the vascularized portion 72 of the meniscus, and moving the unitary surgical device toward the vascularized portion 72, so that the unitary surgical device 10 fills the void 70 in the meniscus. All of the sutures 16, 18, 40, 42, 44, 46 may then be anchored to the back surface 54 of the vascularized portion of the meniscus as shown in FIG. 26. As can be seen from FIG. 26, in this  
25 embodiment the upper projection 80 and under projection 82 both cover the portion of the upper surface 50 between the surfaces 76 and 54 and the portion of the lower surface 88 of the meniscus between the surfaces 76 and 54.

As shown in the embodiment of FIGS. 28-29, the unitary surgical device 10 need not be wedge shaped. The base 21 could comprise a flat sheet with a  
30 pillow or other mass of tissue regeneration material 22 shaped to fill the void 70 left by the menisectomy. The unitary surgical device 10 may then be fixated to the meniscus 12 by using a needle to push the anchoring sutures 16, 18 through the top surface 50 of the meniscus, and then through the body of the meniscus and out

-41-

through the back surface 54 of the meniscus, where the anchoring sutures 16, 18 may be tied, thereby fixating the unitary surgical device to the meniscus. The unitary surgical device 10 of the FIG. 42 embodiment may be fixated in a similar manner.

In addition, as shown in the embodiment of FIGS. 29A-29B, a flat base  
5 21 could be provided with a wedge or otherwise shaped mass of tissue regeneration material 22 fixed to the base. The base 21 could include two fixating members 15, 17 comprising, for example, two lengths of suture 16g, 18g. A third fixating member 77 could also be included in the unitary surgical device. In the embodiment of FIGS. 28A-28B, the third fixating member 77 comprises a backstop and a length of suture  
10 affixed to the mass of tissue regeneration material 22, with the length of suture extending through the mass of tissue regeneration material as in the embodiment of FIGS. 11-12.

As shown in FIG. 27, a unitary surgical device substantially like that shown in FIGS. 28-29 may be provided with barbed darts affixed to the ends of  
15 sutures to define the first and second anchors 16, 18. The unitary surgical device 10 of the FIG. 27 embodiment may be fixated to the meniscus 12 in a manner similar to that shown in FIG. 29, except instead of tying the ends of suture for fixation, the barbed darts 16, 18 may be pressed into the body of the meniscus to thereby fixate the device 10 to the meniscus.

20 The embodiment of FIGS. 30-31 is similar to the embodiment of FIGS. 22-23 and 25-26, except in the embodiment of FIGS. 30-31, each anchor 16, 18, 40, 42, 44, 46 includes a barbed dart at the end of a length of suture. To implant this embodiment, the anchors 16, 18, 40, 42, 44, 46 are moved over and under the portion of the meniscus behind the void 70 and the barbed darts are pushed into the body of  
25 the meniscus through the back 54 of the meniscus. The barbed darts are pushed in until the unitary surgical device is properly fixated. The barbs on the darts prevent the darts from being pulled out.

The embodiment of FIGS. 32-33 is similar to that of FIGS. 20-21, except that instead of using suture as the first and second anchors 16, 18, barbed darts  
30 are affixed to extend outward from the back 74 of the mass of tissue regeneration material 22. To implant this unitary surgical device, the upper and lower projections 80, 82 are moved over and under the surfaces 50, 88 of the vascularized portion 72 of the meniscus behind the void 70 until the barbed darts enter the face 76 of the

-42-

meniscus at the back of the void 70 created during the menisectomy. The barbs on the dart fixate the implant in place against the meniscus. It should be understood that although only one anchoring barbed dart 16 is illustrated in FIGS. 22-23, it is contemplated that more than a single anchoring device may be used in this embodiment. In addition, although the top panel 24 of the base 21 may be affixed to the mass of tissue regeneration material by adhesion, cross-linking, mechanical fixation or the like, the top panel 24 can also be free from such connection and can be surgically fixated to the body of the meniscus as described above with respect to the embodiment of FIGS. 20-21.

10 In the embodiment of FIG. 34, the first and second anchors comprise mating darts and holes. The darts extend upward from the bottom projection 82 and the mating holes are in the upper projection 80. The darts are long enough to extend through the body of part of the meniscus. The embodiment of FIG. 34 may be fixated by placing the device 10 in the void 70 in the meniscus, positioning the bottom projection 82 under part of the meniscus so that the darts extend upward through the meniscus and exit the top of the meniscus. The top panel 24 of the base 21 may then be pressed down so that the tops of the darts extend through the holes and lock the top and bottom portions of the base together and to the meniscus.

20 In the embodiment of FIGS. 35-36, the first and second anchors 16, 18 comprise tacks, and an additional pair of tacks are provided as third and fourth anchors 40, 42. In the embodiment of FIGS. 35-36, the mass of tissue regeneration material 22 is affixed to the top panel 24 of the base 21 by adhesive, cross-linking (chemical or physical) or through mechanical means. The tacks are provided on both the upper and lower projections 80, 82. When implanted, the mass of tissue regeneration material fits within the void 70 left after the menisectomy, and the projections 80, 82 are positioned over and under the upper and lower surfaces 50, 88 of the meniscus 12, between the surfaces 76 and 54 of the meniscus. The tacks extend into the body of the meniscus between the surfaces 76 and 54, thereby fixating the unitary surgical device 10 to the meniscus.

30 In the embodiment of FIGS. 37-38, the unitary surgical device is implanted in a manner similar to the other embodiments. The device 10 is positioned so that the void 70 is substantially filled by the mass of tissue regeneration material 22. Then, the top panel 24 is moved to place the upper projection 80 over the top

-43-

surface 50 of the portion of the meniscus behind the void 70 and the bottom panel is moved to place the lower projection 82 under the lower surface 88 of the meniscus behind the void 70. The female locking member 18 is pushed upward through the lower surface 88 and into the body of the meniscus, and the male locking member 16 is pushed downward through the upper surface 50 into the body of the meniscus until at least part of the male locking member 16 is received in the female locking member 18, thereby fixating the device 10 to the meniscus.

In the embodiment of FIGS. 39-40, the device 10 may be fixated by first implanting the female locking member 18 using a hollow needle delivery system, like that described above for implanting the device 10 of FIGS. 3 and 4. The female locking member 18 is pushed through the surface 76, through the body of the meniscus and out through the surface 54. The suture extends through this passageway and through part of the implant, such as through the mass of tissue regeneration material 22 and through the top panel 24 of the base. The device 10 may be moved into position with the mass of tissue regeneration material located in the void 70 and against the vascularized portion 72 of the meniscus. The male locking member 16 is then pushed into the female locking member, thereby fixating the unitary surgical device 10 to the meniscus 12.

The embodiment of FIG. 50 may be used either as a means of approximating the inner surfaces of a meniscal tear, as shown in FIG. 51, or as a means of fixating a tissue regenerating implant after a partial menisectomy, as shown in FIG. 52. To approximate the surfaces of a tear as shown in FIG. 51, the base 20 (backstop element 19 in FIG. 50) may be inserted using a commercially available device such as a Mitek Meniscal Applier, as described above. Additional standard equipment may then be used to move the first and second anchors 16a, 18c through the non-articulating outer surface 54 of the meniscus, up through the upper articulating surface 50 of the meniscus, across the tear 14, and back into the body of the meniscus until the anchors 16a, 18c are embedded in the meniscus. To fixate a separate tissue regenerating implant as illustrated in FIG. 52, the unitary surgical device 10 of FIG. 50 may be inserted as described above, or could be inserted from the outer, non-articulating side of the meniscus. The anchors 16a, 18c could be pushed through the outer non-articulating surface 54 of the meniscus, through the body of the meniscus, up through the upper articulating surface 50 of the meniscus

-44-

and through the overlying upper portion 80 of the top panel 24 of the implant. The anchors 16a, 18c may then be moved across a portion of the upper surface of the top panel 24 of the implant and back into the body of the outer portion 72 of the meniscus to fixate the implant in place.

5           An additional embodiment of a unitary surgical device is illustrated in FIG. 53. In this embodiment, the upper projection 80 has a plurality of pre-formed holes along the outer edge. Each hole could thereby comprise a fixating member, as shown at 15 and 17 FIG. 53. These holes could be pre-formed in the base 21 so that the surgeon may easily and quickly suture the unitary surgical implant 10 of FIG. 53 to the outer vascular area 72 of the meniscus through the holes 15, 17, as shown in FIG. 53. To implant such a device, the a length of suture, shown at 90 in FIG. 53, with a backstop, shown at 92 in FIG. 53, could be used. The backstop 92 could be positioned against the outer arcuate surface 54 of the meniscus, and then the suture 90 could be stitched to both the unitary surgical device 10 and the vascularized area 72 of the meniscus using, for example, a corkscrew needle (not shown). With such pre-formed holes in the unitary surgical device, there is little risk of damaging the device during implantation.

          Additional surgical techniques can be employed in implanting surgical device of the type described in copending U.S. Patent Application Serial No. XX/XXX,XXX entitled "Meniscus Regeneration Device and Method" (Attorney Docket No. 265280-71141, DEP-745) by Prasanna Malaviya, Herbert Schwartz, David Whalen, Mark Pelo, Phil Jenks, Pamela Plouhar and Jerry Lower.

25           While only specific embodiments of the invention have been described and shown, it is apparent that various alternatives and modifications can be made thereto. Moreover, those skilled in the art will also recognize that certain additions can be made to these embodiments. It is, therefore, the intention in the appended claims to cover all such alternatives, modifications and additions as may fall within the true scope of the invention.

## CLAIMS:

1. A unitary surgical device for implantation in a patient for repairing a body tissue in the patient, the unitary surgical device comprising:
- 5 a first biocompatible anchor including at least one of the following:  
a bioresorbable barbed dart;  
a bioresorbable tack;  
a bioresorbable backstop; and  
a bioresorbable male locking member;
- 10 a second biocompatible anchor including at least one of the following:  
a bioresorbable barbed dart;  
a bioresorbable tack;  
a bioresorbable backstop; and  
a bioresorbable female locking member; and
- 15 biocompatible tissue repair material extending between and connected to the first anchor and to the second anchor prior to surgery, the tissue repair material including at least one of the following:  
a fixed length of suture;  
a sheet of collagen-containing material;
- 20 a sheet of biologically remodelable collagenous matrix;  
laminar ECM material;  
formed ECM material;  
comminuted ECM material;  
ECM fiber;
- 25 ECM foam material;  
cross-linked ECM material;  
a sheet of bioresorbable material; and  
a base and a different material secured to the base, at least one of the base and the different material including ECM material.
- 30 2. The unitary surgical device of claim 1 wherein the tissue repair material includes tissue regeneration material.

-46-

3. The unitary surgical device of claim 2 wherein the tissue regeneration material includes ECM material.

4. The unitary surgical device of claim 3 wherein the ECM material includes material derived from mammalian submucosa.

5 5. The unitary surgical device of claim 1 wherein the ECM material includes material derived from mammalian submucosa.

6. The unitary surgical device of claim 1 wherein at least one of the anchors is sized and shaped to bear against a non-articulating surface of the meniscus of the patient.

10 7. The unitary surgical device of claim 1 wherein the tissue repair material is sized and shaped to extend over a portion of patient's meniscus and to extend over an area from which a portion of the patient's meniscus has been removed.

8. The unitary surgical device of claim 1 wherein the tissue repair material is wedge-shaped in cross-section.

15 9. The unitary surgical device of claim 1 wherein the tissue repair material further includes suture and a backstop.

10. The unitary surgical device of claim 1 further comprising a package holding the unitary surgical device.

20 11. A unitary surgical device for surgical implantation in a patient for regenerating fibrocartilage tissue in the patient, the unitary surgical device comprising:

a first fixating mechanism including at least one of the following:

a length of suture;

a bioresorbable barbed dart;

25 a bioresorbable tack;

a bioresorbable backstop; and

a bioresorbable male locking member;

a second fixating mechanism including at least one of the following:

a length of suture;

30 a bioresorbable barbed dart;

a bioresorbable tack;

a bioresorbable backstop; and

a bioresorbable female locking member; and

-47-

tissue repair material connected to the first fixating mechanism and the second fixating mechanism prior to surgery, the tissue repair material including at least one of the following:

5 a sheet of ECM material connected to the first fixating mechanism and the second fixating mechanism;

laminar ECM material connected to the first fixating mechanism and the second fixating mechanism;

ECM foam;

comminuted ECM;

10 ECM fiber;

cross-linked ECM material;

formed ECM material; and

a bioresorbable base and a different material on the base, at least one of the base and the different material including ECM.

15 12. The unitary surgical device of claim 11 wherein the ECM material comprises mammalian submucosa.

13. The unitary surgical device of claim 11 wherein the base comprises at least one of the following:

a sheet of ECM material;

20 laminar ECM material;

formed ECM material;

cross-linked ECM;

woven ECM;

non-woven ECM;

25 braided ECM;

ECM foam;

a sheet of biocompatible polymer;

laminar biocompatible polymer;

formed biocompatible polymer;

30 cross-linked biocompatible polymer;

woven biocompatible polymer;

non-woven biocompatible polymer;

knitted biocompatible polymer;



-48-

warp-knitted biocompatible polymer;  
braided biocompatible polymer; and  
biocompatible foam.

14. The unitary surgical device of claim 13 wherein the ECM  
5 material is derived from mammalian submucosa.

15. The unitary surgical device of claim 11 wherein the  
bioresorbable base comprises two faces meeting at an apex and wherein the different  
material comprises ECM material positioned between said two faces.

16. The unitary surgical device of claim 15 wherein the tissue  
10 repair material is wedge-shaped in cross-section.

17. The unitary surgical device of claim 11 wherein the different  
material on the base includes at least one of the following:

ECM foam;  
ECM fibers;  
15 ECM powder;  
comminuted ECM;  
ECM threads;  
ECM wovens;  
ECM non-wovens;  
20 braided ECM;  
ECM solutions;  
ECM gel;  
ECM paste; and  
cross-linked ECM.

18. The unitary surgical device of claim 11 further comprising a  
25 package holding the unitary surgical device.

19. A unitary surgical device for surgical implantation in a patient  
for regenerating fibrocartilage tissue in the patient, the unitary surgical device  
comprising:

30 a base having at least two layers;  
a length of suture positioned between two of the layers of the base;  
at least part of the unitary surgical device being made from ECM  
material.

-49-

20. The unitary surgical device of claim 19 wherein at least part of the unitary surgical device is made from a biocompatible bioresorbable polymer.

21. The unitary surgical device of claim 19 wherein the length of suture includes two exposed ends, the unitary surgical device further comprising an anchor at each exposed end of the suture.

22. A unitary surgical device for surgical implantation in a patient for regenerating meniscal tissue in the patient, the unitary surgical device comprising:  
a base having two panels in a V-shaped configuration in cross-section, the two panels meeting along an apex portion and having end portions spaced distally from the apex portion, the end portions being spaced from each other to provide a gap;

tissue regeneration material between the two panels of the base; and opposing anchors on the end portions of the base panels, the opposing anchors being suitable for fixation to the native meniscus.

23. The unitary surgical device of claim 22 wherein the tissue regeneration material comprises a wedge of ECM material.

24. A unitary surgical device for surgical implantation in a patient for regenerating tissue in the patient, the unitary surgical device comprising:  
a base made of a bioresorbable polymer;  
ECM material on the base; and  
a first fixating member secured to the base prior to surgery, the first fixating member being suitable for fixation to the patient's tissue.

25. The unitary surgical device of claim 24 wherein the first fixating member includes at least one of the following: a length of bioresorbable suture; a bioresorbable barbed dart; a bioresorbable tack; a bioresorbable backstop; and a bioresorbable locking member.

26. The unitary surgical device of claim 24 wherein the ECM material includes at least one of the following:

ECM foam;  
ECM fibers;  
ECM powder;  
ECM threads;  
ECM wovens;

-50-

ECM non-wovens;  
braided ECM;  
ECM solutions;  
ECM gel;  
5 ECM paste; and  
cross-linked ECM.

27. The unitary surgical device of claim 24 wherein the base further comprises ECM material.

28. The unitary surgical device of claim 24 further comprising a  
10 second fixating member secured to the base prior to surgery, the second fixating member being suitable for fixation to the patient's tissue and including at least one of the following: a length of bioresorbable suture; a bioresorbable barbed dart; a bioresorbable tack; a bioresorbable backstop; and a bioresorbable locking member.

29. A unitary surgical device for surgical implantation in a patient  
15 for regenerating tissue in the patient, the unitary surgical device comprising:  
a base made of ECM material; and  
a first fixating member secured to the base prior to surgery, the first fixating member being suitable for fixation to the patient's tissue.

30. The unitary surgical device of claim 29 wherein the first  
20 fixating member includes at least one of the following: a length of bioresorbable suture; a bioresorbable barbed dart; a bioresorbable tack; a bioresorbable backstop; and a bioresorbable locking member.

31. The unitary surgical device of claim 29 wherein the ECM  
material includes at least one of the following:

25 laminar ECM;  
formed ECM;  
ECM foam;  
ECM fibers;  
ECM wovens;  
30 ECM non-wovens;  
braided ECM; and  
cross-linked ECM.

-51-

32. The unitary surgical device of claim 29 wherein the base further comprises tissue regeneration material secured to the base, the tissue regeneration material including at least one of the following:

- ECM foam;
- 5 ECM fibers;
- ECM powder;
- ECM threads;
- ECM wovens;
- ECM non-wovens;
- 10 braided ECM;
- ECM solutions;
- ECM gel;
- ECM paste; and
- cross-linked ECM.

15 33. The unitary surgical device of claim 29 further comprising a second fixating member secured to the base prior to surgery, the second fixating member being suitable for fixation to the patient's tissue and including at least one of the following: a length of bioresorbable suture; a bioresorbable barbed dart; a bioresorbable tack; a bioresorbable backstop; and a bioresorbable locking member.

20 34. A unitary surgical device for surgical implantation in a patient for regenerating tissue in the patient, the unitary surgical device comprising:  
a base having two opposing edges and a plurality of holes along one of the edges of the base; and

ECM material positioned between the two opposing edges of the base.

25 35. A unitary surgical device for surgical implantation in a patient for regenerating meniscal tissue in the patient, the unitary surgical device comprising:

a base comprising a panel with upper and lower surfaces; and  
generally wedge-shaped tissue regeneration material fixed to at least one of the surfaces of the base; and

30 a fixating member associated with at least one of the base and the generally wedge-shaped tissue regeneration material.

36. The unitary surgical device of claim 35 wherein the fixating member includes at least one of the following:

-52-

a length of suture fixed to the base;  
at least one hole in the base;  
a biocompatible anchor fixed to the base;  
a biocompatible anchor fixed to the tissue regeneration material; and  
a length of suture fixed to the tissue regeneration material.

5

37. A method of repairing a tear in the meniscus in the knee of a patient, the meniscus having an articulating surface and a non-articulating surface, the tear resulting in the meniscus having two inner surfaces, the method comprising the acts of:

10

providing a unitary surgical device having a pair of resorbable anchors and a fixed length of suture connecting each of the anchors;

locating the tear in the meniscus;

implanting the unitary surgical device to approximate the two inner surfaces of the meniscus at the tear, with suture extending across the articulating surface of the meniscus across the tear and the resorbable anchors being spaced from the tear.

15

38. The method of claim 37 wherein at least one of the resorbable anchors is positioned against a non-articulating surface of the meniscus.

39. A method of repairing a damaged meniscus in the knee of a patient, the meniscus having a non-articulating surface, a peripheral rim and an inner portion, the method comprising the acts of:

20

providing a generally wedge-shaped unitary surgical device including a fixating mechanism;

removing a portion of the damaged meniscus inward of the peripheral rim of the meniscus;

25

implanting the unitary surgical device with a portion inward of the peripheral rim; and

fixating the unitary surgical device to the meniscus by fixating at least part of the base of the unitary surgical device to the meniscus with the fixating mechanism.

30

40. A method of repairing a torn meniscus in the knee of a patient, the torn meniscus having two adjacent non-articulating surface, a peripheral rim and an inner portion, the method comprising the acts of:

-53-

providing a unitary surgical device including a base with two opposite surfaces;

implanting the unitary surgical device between the two adjacent non-articulating surfaces of the torn meniscus; and

5       fixating the unitary surgical device to the meniscus with one surface of the unitary surgical device being juxtaposed with one of the two adjacent non-articulating surfaces of the torn meniscus and the other surface of the unitary surgical device being juxtaposed with the other of the two adjacent non-articulating surfaces of the torn meniscus.

10       41.     The method of claim 40 wherein the unitary surgical device includes ECM material.

42.     A method of preparing a unitary surgical device for use in surgery comprising the acts of:

15       providing a first biocompatible anchor including at least one of the following:

a bioresorbable barbed dart;  
a bioresorbable tack;  
a bioresorbable backstop; and  
a bioresorbable male locking member;

20       providing a second biocompatible anchor including at least one of the following:

a bioresorbable barbed dart;  
a bioresorbable tack;  
a bioresorbable backstop; and  
a bioresorbable female locking member; and

25       providing a biocompatible tissue repair material including at least one of the following:

a fixed length of suture;  
a sheet of collagen-containing material;  
30       laminar ECM material;  
formed ECM material;  
comminuted ECM material;  
ECM fiber;

-54-

ECM foam material;  
cross-linked ECM material;  
a sheet of bioresorbable material; and  
a base and a different material secured to the base, at least one of the  
5 base and the different material including ECM material;  
securing the biocompatible tissue repair material to the first anchor and  
to the second anchor to form a unitary device; and  
sterilizing the unitary surgical device.

43. The method of claim 42 further comprising packaging the  
10 unitary surgical device prior to sterilizing the unitary surgical device.

44. The method of claim 42 further comprising:  
providing a third biocompatible anchor including at least one of the  
following:

15 a bioresorbable barbed dart;  
a bioresorbable tack;  
a bioresorbable backstop; and  
a bioresorbable male locking member;  
providing a fourth biocompatible anchor including at least one of the  
following:

20 a bioresorbable barbed dart;  
a bioresorbable tack;  
a bioresorbable backstop; and  
a bioresorbable female locking member; and  
providing additional biocompatible tissue repair material including at  
25 least one of the following:

30 a fixed length of suture;  
a sheet of collagen-containing material;  
laminar ECM material;  
formed ECM material;  
comminuted ECM material;  
ECM fiber;  
ECM foam material;  
cross-linked ECM material;

-55-

a sheet of bioresorbable material; and  
a base and a different material secured to the base, at least one of the  
base and the different material including ECM material;  
securing the additional biocompatible tissue repair material to the third  
5 anchor and to the fourth anchor to form a second unitary device; and  
packaging the two unitary surgical devices together prior to  
sterilization.

45. A method of preparing a unitary surgical device for use in  
surgery comprising the acts of:  
10 providing a fixating mechanism including at least one of the following:  
a length of suture;  
a bioresorbable barbed dart;  
a bioresorbable tack;  
a bioresorbable backstop; and  
15 a bioresorbable male locking member;  
providing tissue repair material including at least one of the following:  
a sheet of ECM material;  
laminar ECM material;  
ECM foam;  
20 comminuted ECM;  
ECM fiber;  
cross-linked ECM material;  
formed ECM material; and  
a bioresorbable base and a different material on the base, at least one  
25 of the base and the different material including ECM;  
securing the fixating mechanism to the tissue repair material to form a  
unitary surgical device; and  
sterilizing the unitary surgical device.

46. The method of claim 45 further comprising packaging the  
30 unitary surgical device prior to sterilizing the unitary surgical device.

47. The method of claim 45 further comprising:  
providing an additional fixating mechanism including at least one of  
the following:



-56-

5 a length of suture;  
a bioresorbable barbed dart;  
a bioresorbable tack;  
a bioresorbable backstop; and  
a bioresorbable male locking member;  
providing additional tissue repair material including at least one of the

following:

10 a sheet of ECM material;  
laminar ECM material;  
ECM foam;  
comminuted ECM;  
ECM fiber;  
cross-linked ECM material;  
formed ECM material; and  
15 a bioresorbable base and a different material on the base, at least one  
of the base and the different material including ECM;  
securing the additional fixating mechanism to the additional tissue  
repair material to form a second unitary surgical device; and  
packaging the two unitary surgical devices together as a unit prior to  
20 sterilization.

48. A method of preparing a unitary surgical device for use in  
surgery comprising the acts of:

25 providing ECM material;  
providing a fixating mechanism;  
securing the ECM material and the fixating mechanism together to  
form the unitary surgical device; and  
sterilizing the unitary surgical device.

49. The method of claim 48 further comprising packaging the  
unitary surgical device prior to sterilizing the unitary surgical device.

30 50. The method of claim 48 further comprising:  
providing additional ECM material;  
providing an additional fixating mechanism;

-57-

securing the additional ECM material and the additional fixating mechanism together to form a second unitary surgical device; and packaging the two unitary surgical devices together prior to sterilization.

- 5            51.     The method of claim 48 wherein:  
the fixating mechanism includes at least one of the following:  
a length of suture;  
a bioresorbable barbed dart;  
a bioresorbable tack;  
10           a bioresorbable backstop; and  
a bioresorbable male locking member; and  
the ECM material includes at least one of the following:  
a sheet of ECM material;  
laminar ECM material;  
15           ECM foam;  
woven ECM;  
non-woven ECM matt;  
braided ECM;  
ECM fiber;  
20           cross-linked ECM material;  
formed ECM material; and

52.     A method of making a unitary surgical device for use in surgery comprising the acts of:

- providing an ECM material;  
25           providing a biocompatible polymer;  
             providing a fixating mechanism;  
             securing the ECM material, biocompatible polymer and fixating mechanism together to form a unitary surgical device; and  
             sterilizing the unitary surgical device.

30           53.     The method of claim 52 further comprising packaging the unitary surgical device prior to sterilization.

54.     The method of claim 52 further comprising:  
providing additional ECM material;

-58-

providing additional biocompatible polymer;  
providing an additional fixating mechanism;  
securing the additional ECM material, biocompatible polymer and  
fixating mechanism together to form a second unitary surgical device; and  
5 packaging the two unitary surgical devices together prior to  
sterilization.

55. A unitary surgical device for implantation in a patient for  
repairing a body tissue in the patient, the unitary surgical device comprising:

- 10 a first biocompatible anchor including at least one of the following:  
a bioresorbable barbed dart;  
a bioresorbable tack;  
a bioresorbable backstop; and  
a bioresorbable male locking member;  
a second biocompatible anchor including at least one of the following:  
15 a bioresorbable barbed dart;  
a bioresorbable tack;  
a bioresorbable backstop; and  
a bioresorbable female locking member; and  
biocompatible tissue repair material extending between and connected  
20 to the first anchor and to the second anchor prior to surgery, the tissue repair material  
including at least one of the following:  
a fixed length of suture;  
a sheet of bioremodelable collagenous matrix;  
bioremodelable collagenous tissue matrix having a density greater than  
25  $0.5 \text{ g/cm}^3$  connected to the first fixating mechanism and the second fixating  
mechanism;  
bioremodelable collagenous tissue matrix having a density greater than  
 $0.7 \text{ g/cm}^3$  connected to the first fixating mechanism and the second fixating  
mechanism;  
30 bioremodelable collagenous tissue matrix having a density greater than  
 $0.9 \text{ g/cm}^3$  connected to the first fixating mechanism and the second fixating  
mechanism;  
bioremodelable collagenous tissue matrix seeded with cells;

-59-

bioremodelable collagenous tissue matrix combined with a biological lubricant;

formed bioremodelable collagenous tissue matrix material;

pieces of bioremodelable collagenous tissue matrix;

5 bioremodelable collagenous tissue matrix foam;

cross-linked bioremodelable collagenous tissue matrix;

a sheet of bioresorbable material; and

a base and a different material secured to the base, at least one of the base and the different material including bioremodelable collagenous tissue matrix.

10 56. A unitary surgical device for surgical implantation in a patient for regenerating fibrocartilage tissue in the patient, the unitary surgical device comprising:

a first fixating mechanism including at least one of the following:

a length of suture;

15 a bioresorbable barbed dart;

a bioresorbable tack;

a bioresorbable backstop; and

a bioresorbable male locking member;

a second fixating mechanism including at least one of the following:

20 a length of suture;

a bioresorbable barbed dart;

a bioresorbable tack;

a bioresorbable backstop; and

a bioresorbable female locking member; and

25 tissue repair material connected to the first fixating mechanism and the second fixating mechanism prior to surgery, the tissue repair material including at least one of the following:

a sheet of bioremodelable collagenous tissue matrix connected to the first fixating mechanism and the second fixating mechanism;

30 bioremodelable collagenous tissue matrix having a density greater than 0.5 g/cm<sup>3</sup> connected to the first fixating mechanism and the second fixating mechanism;

-60-

bioremodelable collagenous tissue matrix having a density greater than  $0.7 \text{ g/cm}^3$  connected to the first fixating mechanism and the second fixating mechanism;

5 bioremodelable collagenous tissue matrix having a density greater than  $0.9 \text{ g/cm}^3$  connected to the first fixating mechanism and the second fixating mechanism;

bioremodelable collagenous tissue matrix seeded with cells;  
bioremodelable collagenous tissue matrix combined with a biological lubricant;

10 bioremodelable collagenous tissue matrix foam;  
pieces of bioremodelable collagenous tissue matrix;  
cross-linked bioremodelable collagenous tissue matrix;  
formed bioremodelable collagenous tissue matrix; and  
a bioresorbable base and a different material on the base, at least one  
15 of the base and the different material including bioremodelable collagenous tissue matrix.

57. A unitary surgical device for surgical implantation in a patient for regenerating fibrocartilage tissue in the patient, the unitary surgical device comprising:

20 a base having at least two layers;  
a length of suture positioned between two of the layers of the base;  
at least part of the unitary surgical device being made from naturally occurring bioremodelable collagenous tissue matrix.

58. A unitary surgical device for surgical implantation in a patient  
25 for regenerating tissue in the patient, the unitary surgical device comprising:

a base made of a bioresorbable polymer;  
a bioremodelable collagenous tissue matrix on the base; and  
a first fixating member secured to the base prior to surgery, the first fixating member being suitable for fixation to the patient's tissue.

30 59. A unitary surgical device for surgical implantation in a patient for regenerating tissue in the patient, the unitary surgical device comprising:

a base made of naturally occurring bioremodelable collagenous tissue matrix material; and

-61-

a first fixating member secured to the base prior to surgery, the first fixating member being suitable for fixation to the patient's tissue.

60. A unitary surgical device for surgical implantation in a patient for regenerating tissue in the patient, the unitary surgical device comprising:

5 a base having two opposing edges and a plurality of holes along one of the edges of the base; and

bioremodelable collagenous tissue matrix material positioned between the two opposing edges of the base.

61. A method of preparing a unitary surgical device for use in surgery comprising the acts of:

10 providing a first biocompatible anchor including at least one of the following:

a bioresorbable barbed dart;

a bioresorbable tack;

15 a bioresorbable backstop; and

a bioresorbable male locking member;

providing a second biocompatible anchor including at least one of the following:

a bioresorbable barbed dart;

20 a bioresorbable tack;

a bioresorbable backstop; and

a bioresorbable female locking member; and

providing a biocompatible tissue repair material including at least one of the following:

25 a fixed length of suture;

a sheet of collagen-containing material;

laminar bioremodelable collagenous tissue matrix;

formed bioremodelable collagenous tissue matrix;

comminuted bioremodelable collagenous tissue matrix;

30 bioremodelable collagenous tissue matrix fiber;

bioremodelable collagenous tissue matrix foam;

cross-linked bioremodelable collagenous tissue matrix;

a sheet of bioresorbable material; and

-62-

a base and a different material secured to the base, at least one of the base and the different material including bioremodelable collagenous tissue matrix material;

5       securing the biocompatible tissue repair material to the first anchor and to the second anchor to form a unitary device; and  
sterilizing the unitary surgical device.

62.     A method of preparing a unitary surgical device for use in surgery comprising the acts of:

10       providing a fixating mechanism including at least one of the following:  
a length of suture;  
a bioresorbable barbed dart;  
a bioresorbable tack;  
a bioresorbable backstop; and  
a bioresorbable male locking member;  
15       providing tissue repair material including at least one of the following:  
bioremodelable collagenous tissue matrix seeded with cells;  
bioremodelable collagenous tissue matrix combined with a biological  
lubricant;  
a sheet of bioremodelable collagenous tissue matrix;  
20       laminar bioremodelable collagenous tissue matrix;  
bioremodelable collagenous tissue matrix foam;  
pieces of bioremodelable collagenous tissue matrix;  
cross-linked bioremodelable collagenous tissue matrix;  
bioremodelable collagenous tissue matrix having a density greater than  
25       0.5 g/cm<sup>3</sup>;  
bioremodelable collagenous tissue matrix having a density greater than  
0.7 g/cm<sup>3</sup>;  
bioremodelable collagenous tissue matrix having a density greater than  
0.9 g/cm<sup>3</sup>;  
30       formed bioremodelable collagenous tissue matrix; and  
a bioresorbable base and a different material on the base, at least one of the base and the different material including bioremodelable collagenous tissue matrix;

-63-

securing the fixating mechanism to the tissue repair material to form a unitary surgical device; and

sterilizing the unitary surgical device.

63. A method of preparing a unitary surgical device for use in  
5 surgery comprising the acts of:

providing bioremodelable collagenous tissue matrix;

providing a fixating mechanism;

securing the bioremodelable collagenous tissue matrix and the fixating  
mechanism together to form the unitary surgical device; and

10 sterilizing the unitary surgical device.

64. A method of making a unitary surgical device for use in  
surgery comprising the acts of:

providing a bioremodelable collagenous tissue matrix;

providing a biocompatible polymer;

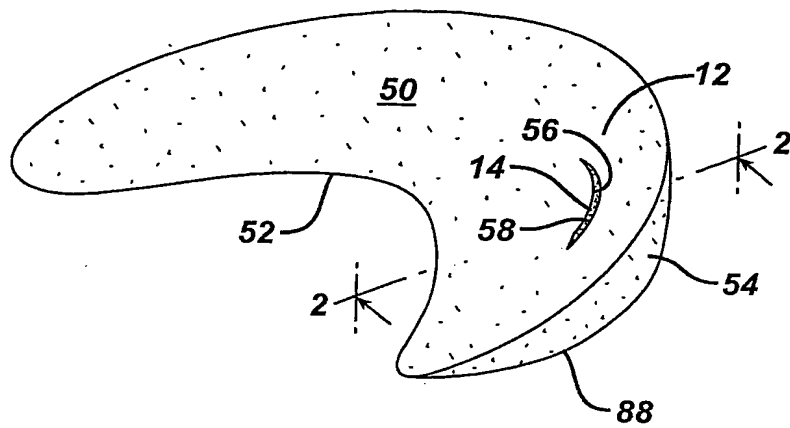
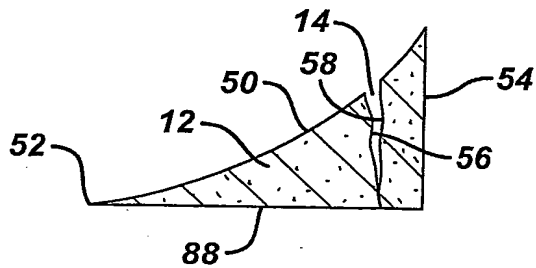
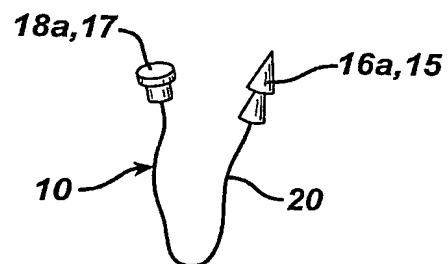
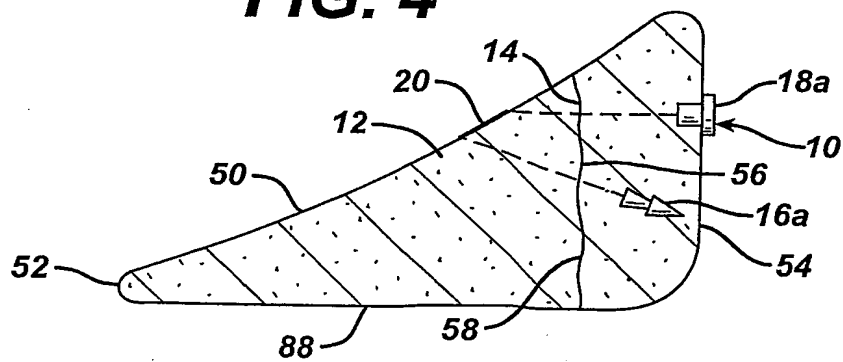
15 providing a fixating mechanism;

securing the bioremodelable collagenous tissue matrix, biocompatible  
polymer and fixating mechanism together to form a unitary surgical device; and

sterilizing the unitary surgical device.

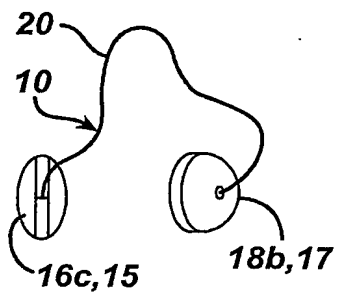


1/18

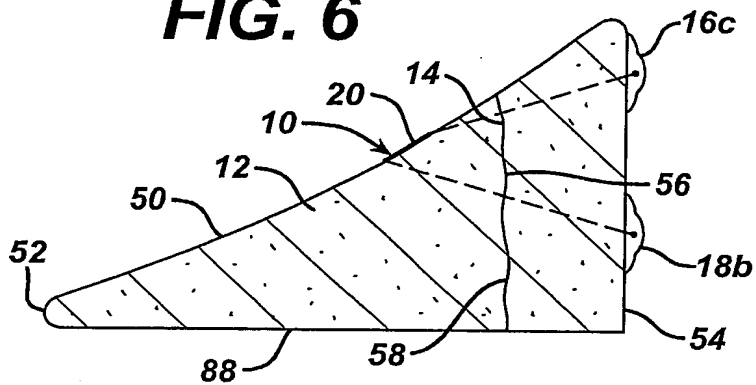
**FIG. 1****FIG. 2****FIG. 3****FIG. 4**

2/18

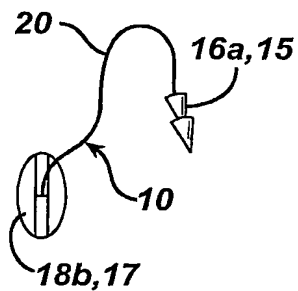
**FIG. 5**



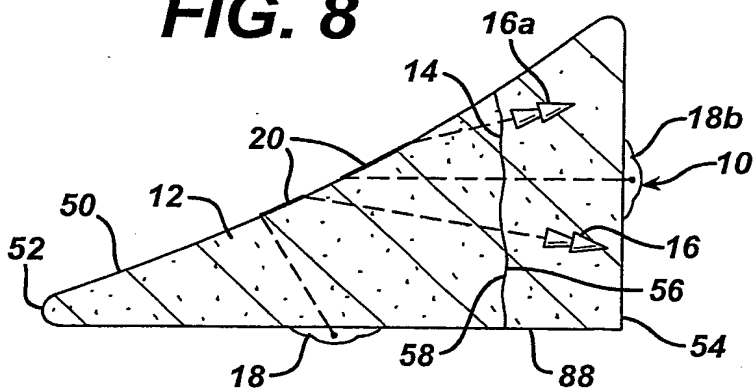
**FIG. 6**



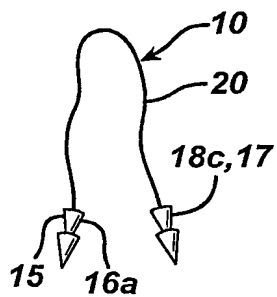
**FIG. 7**



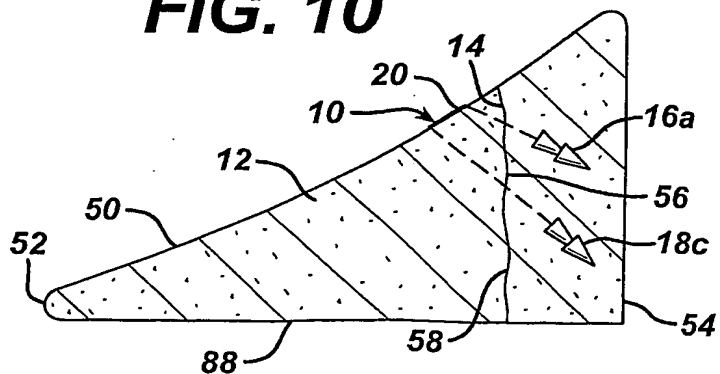
**FIG. 8**



**FIG. 9**

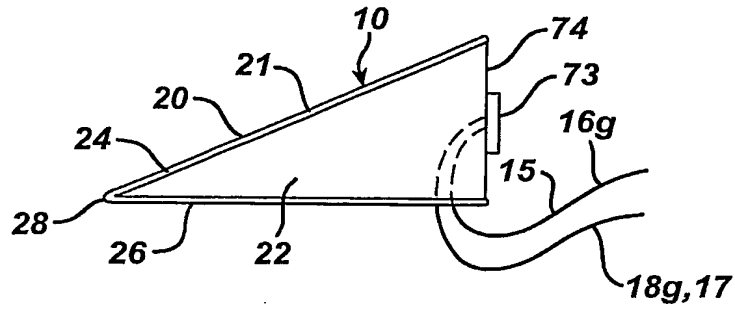


**FIG. 10**

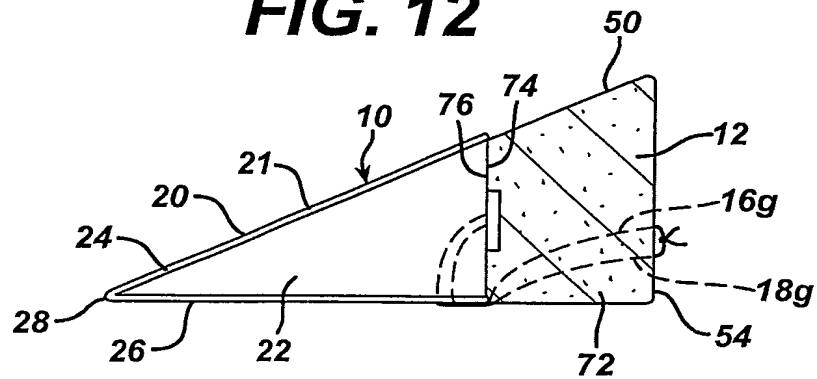


3/18

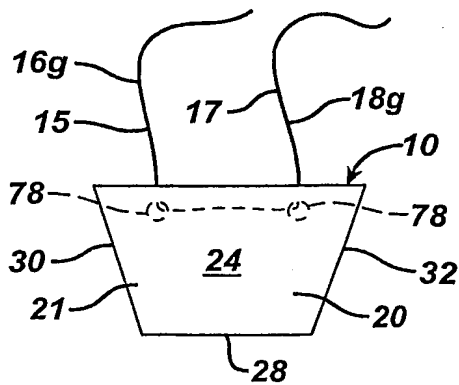
**FIG. 11**



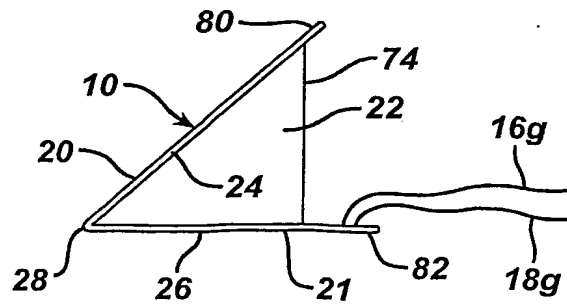
**FIG. 12**



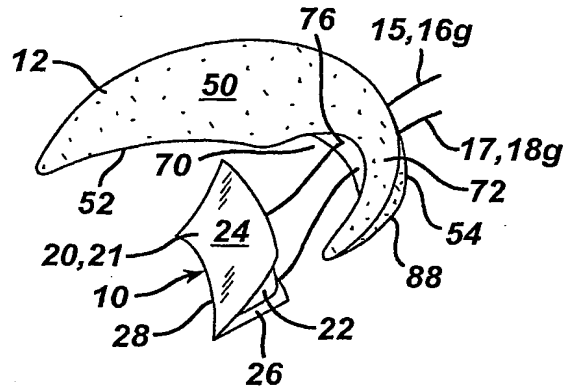
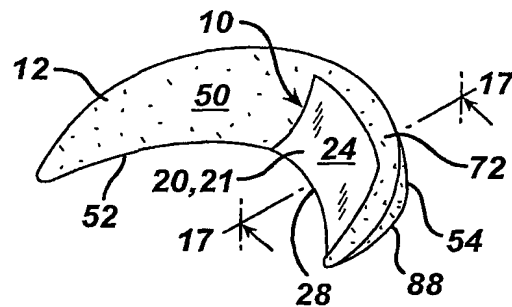
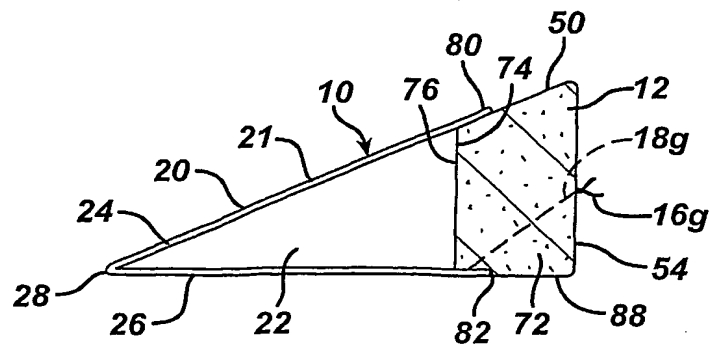
**FIG. 13**



**FIG. 14**

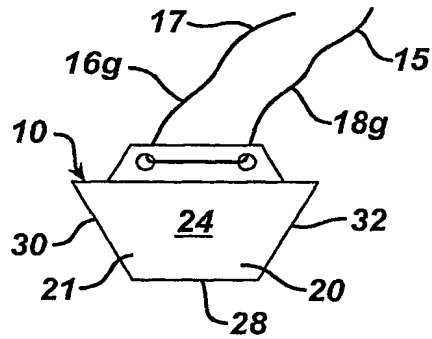


4/18

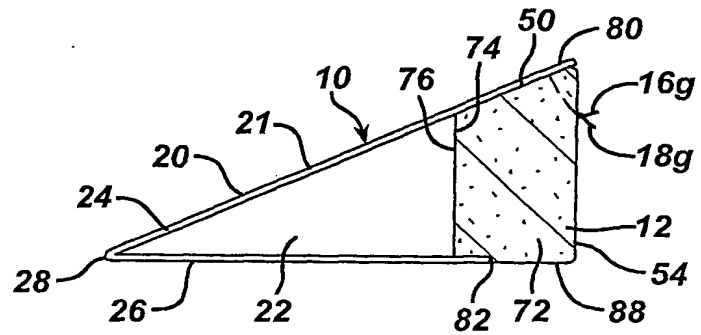
**FIG. 15****FIG. 16****FIG. 17**

5/18

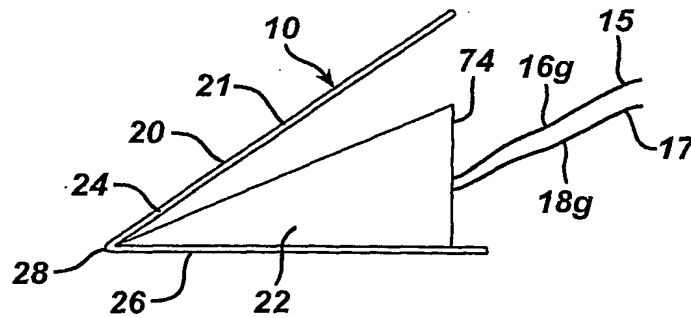
**FIG. 18**



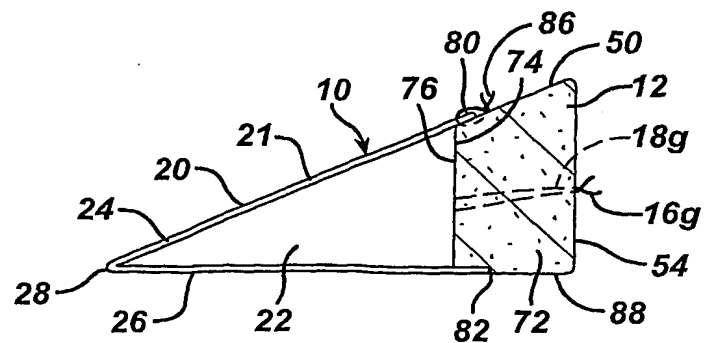
**FIG. 19**



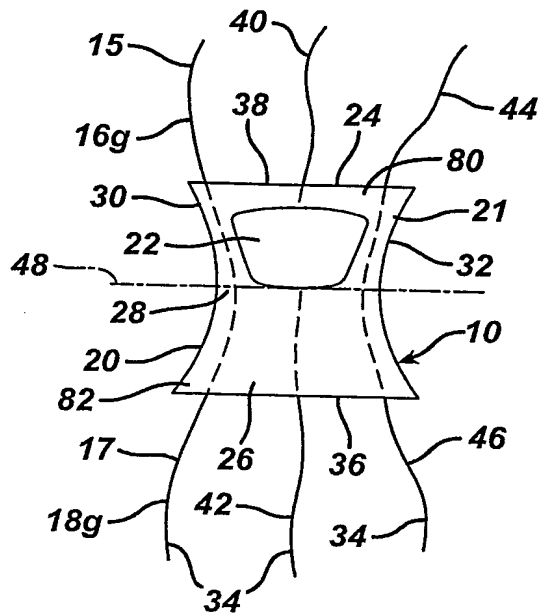
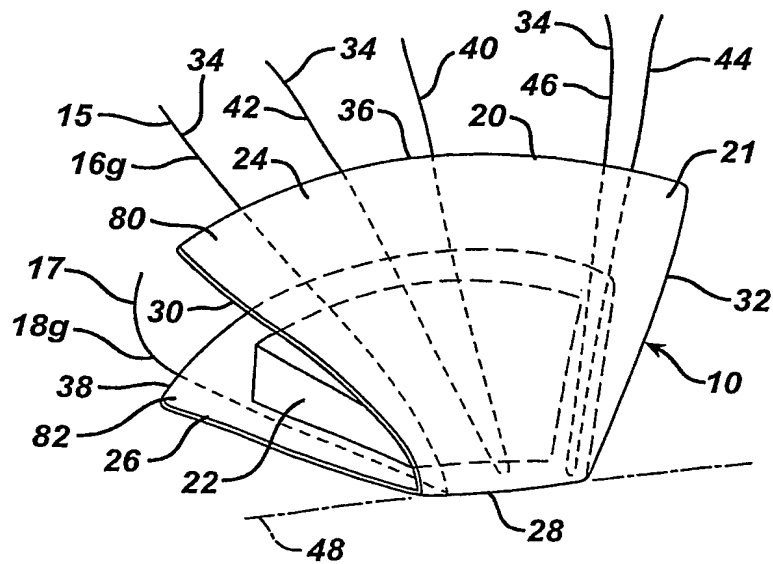
**FIG. 20**



**FIG. 21**

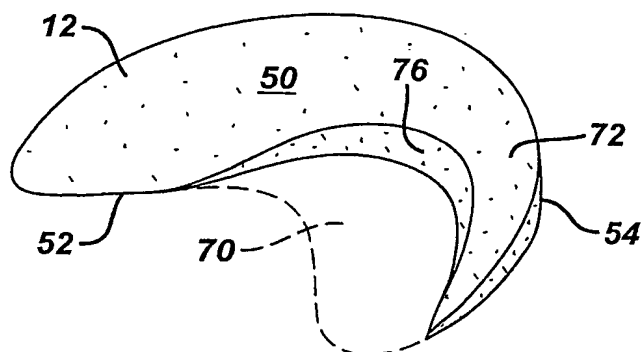


6/18

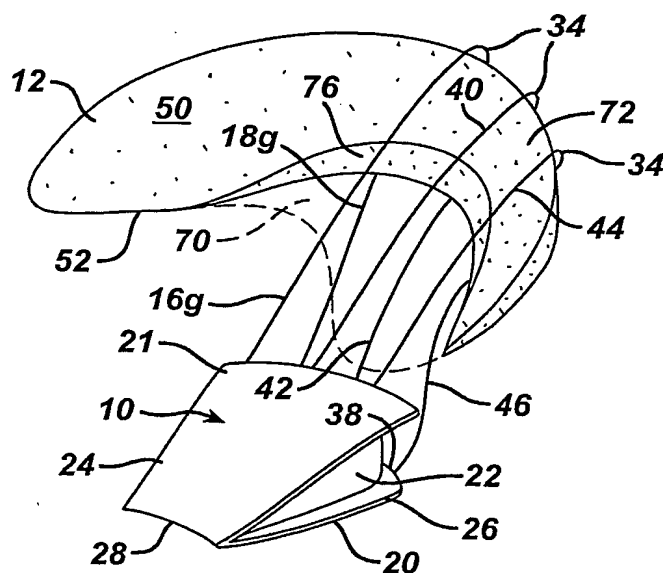
**FIG. 22****FIG. 23**

7/18

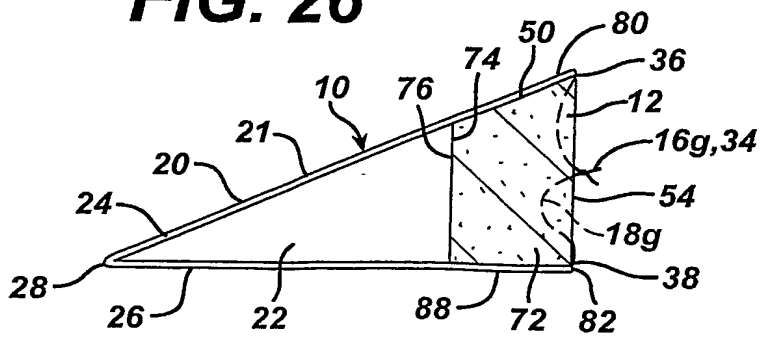
**FIG. 24**



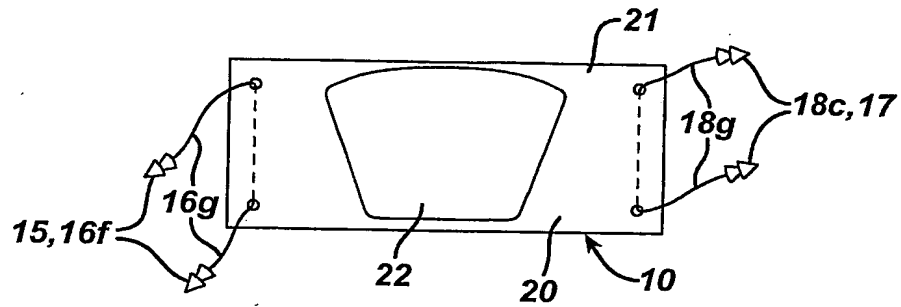
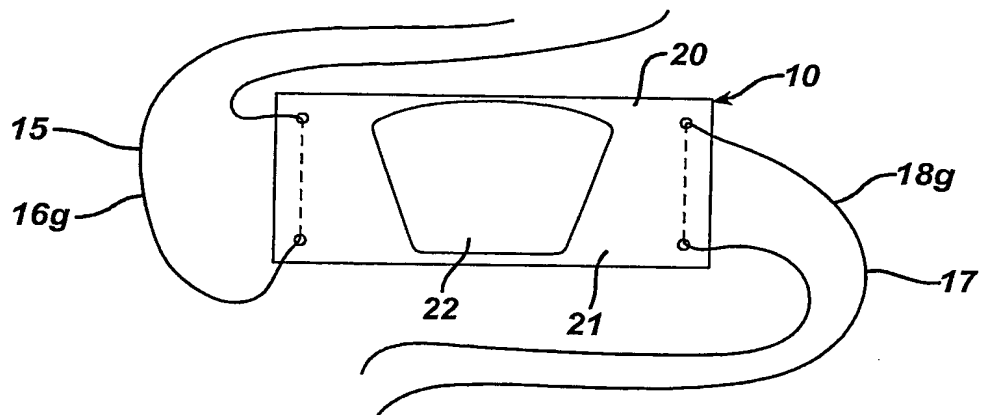
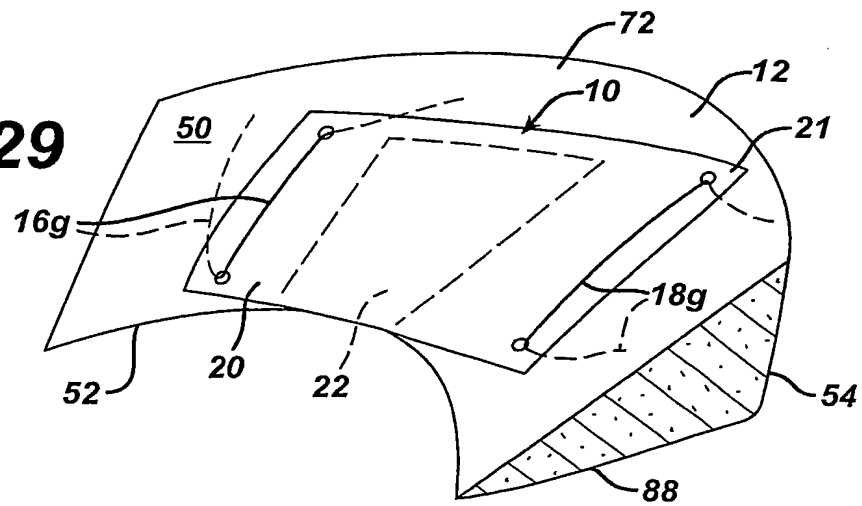
**FIG. 25**



**FIG. 26**



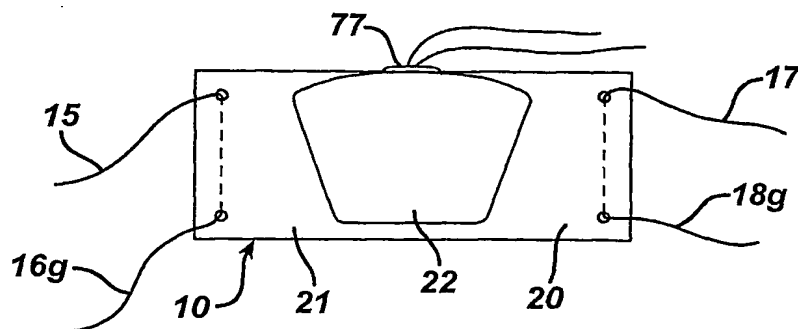
8/18

**FIG. 27****FIG. 28****FIG. 29**

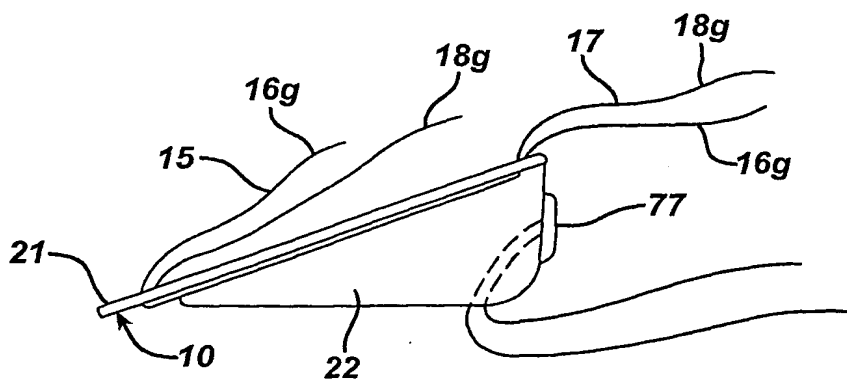


9/18

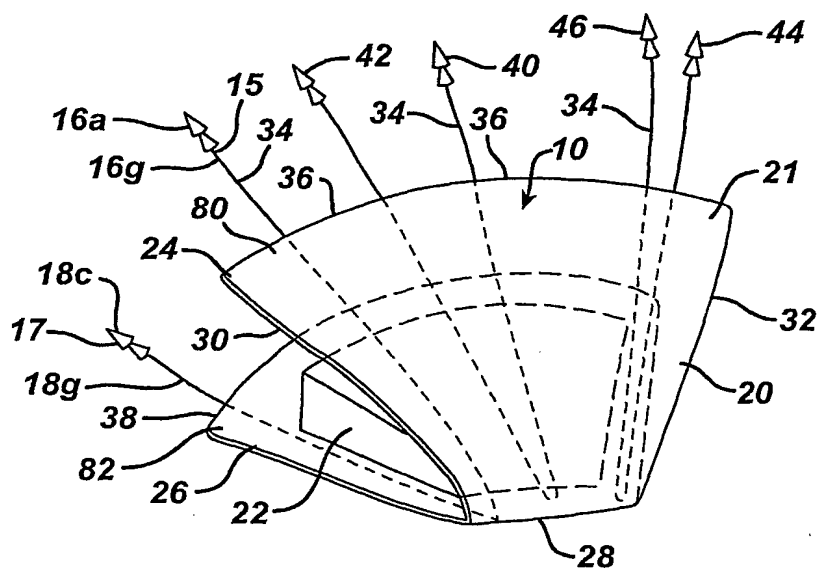
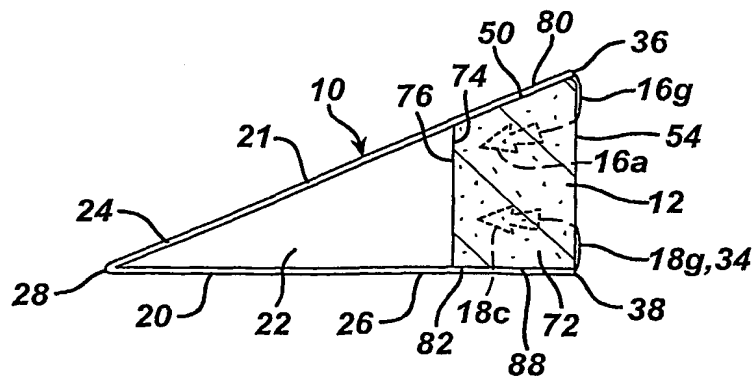
**FIG. 29A**



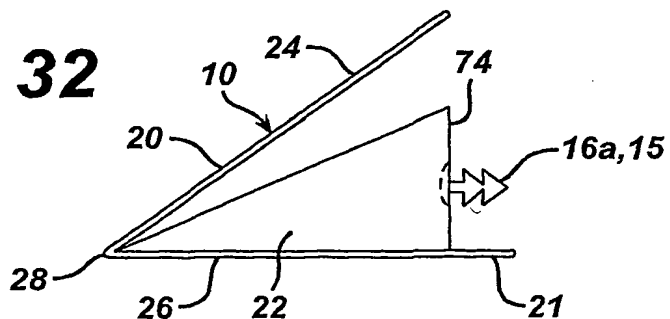
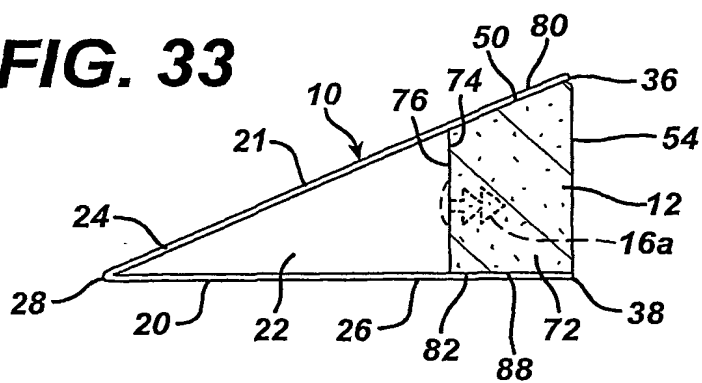
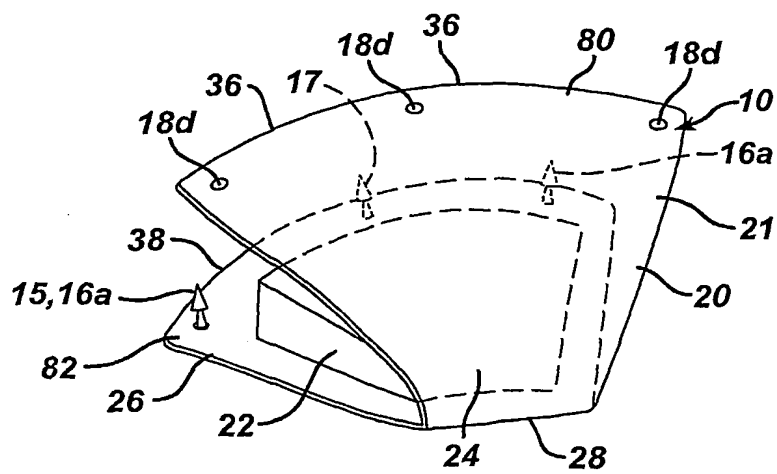
**FIG. 29B**



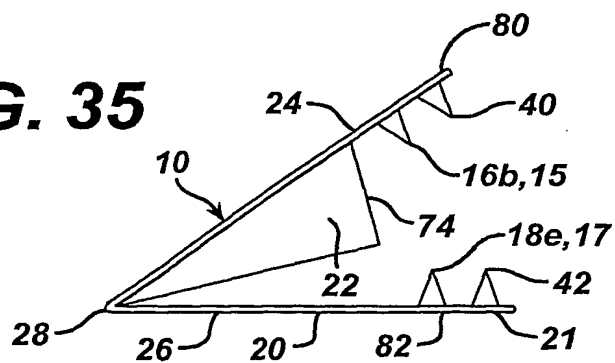
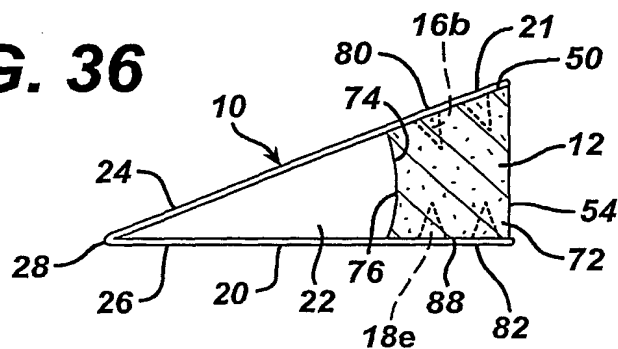
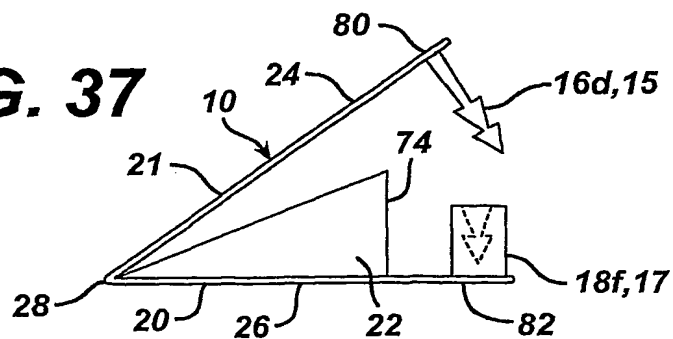
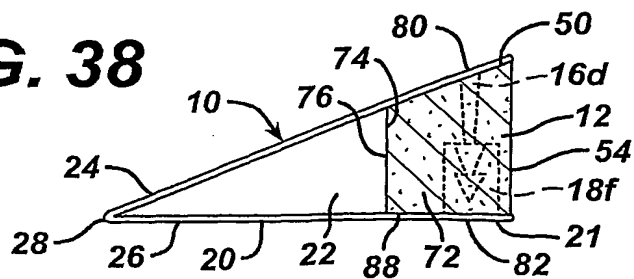
10/18

**FIG. 30****FIG. 31**

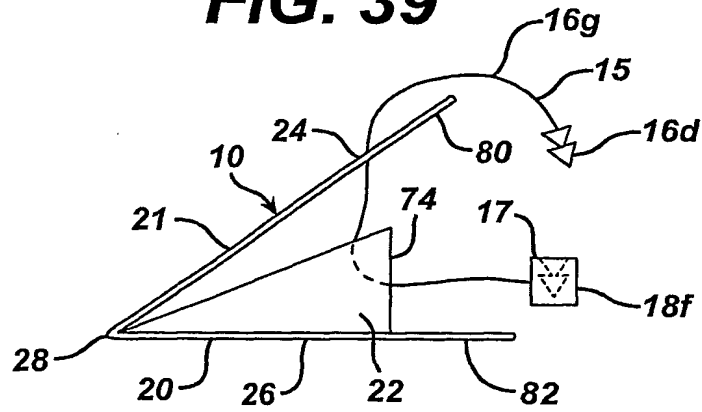
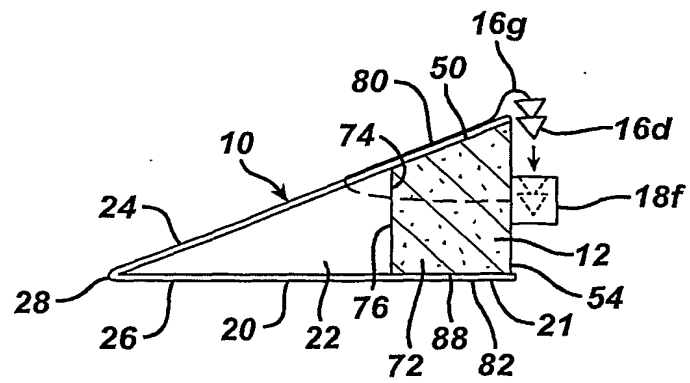
11/18

**FIG. 32****FIG. 33****FIG. 34**

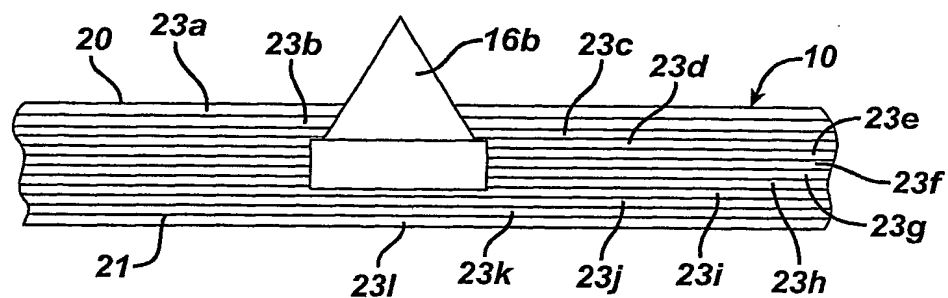
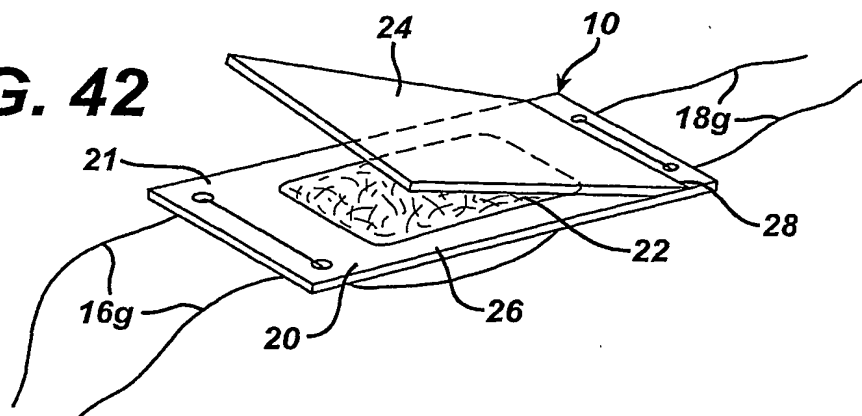
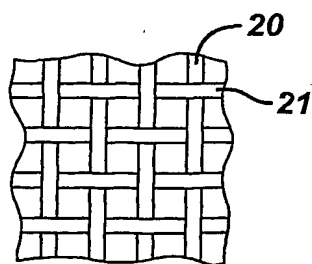
12/18

**FIG. 35****FIG. 36****FIG. 37****FIG. 38**

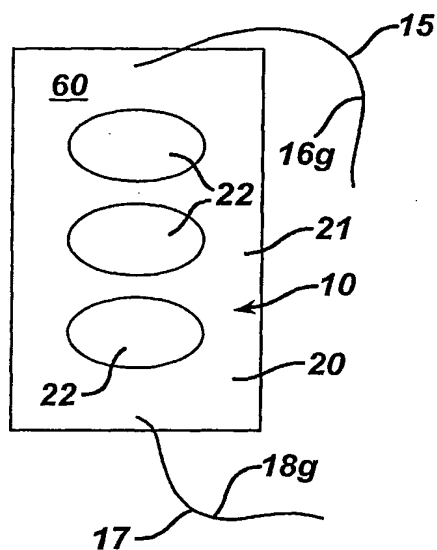
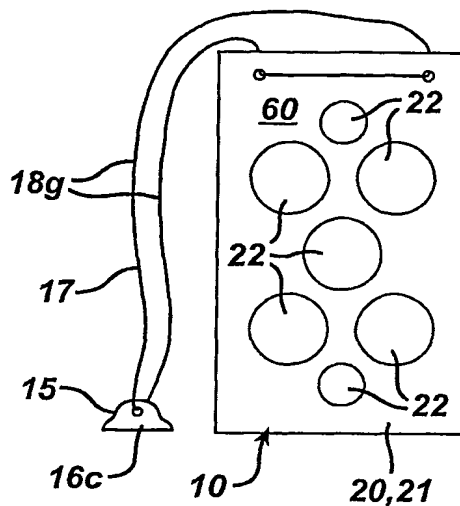
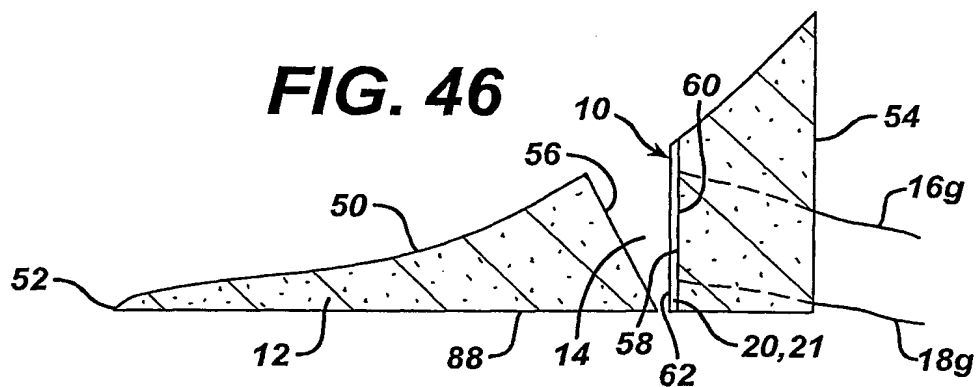
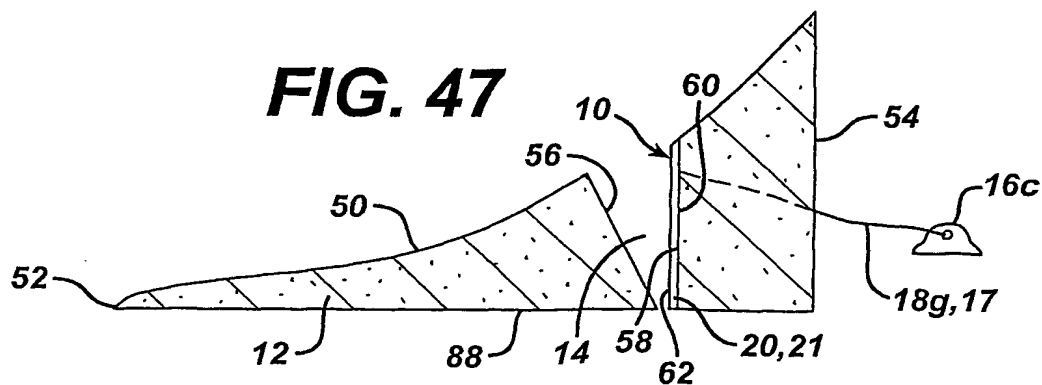
13/18

**FIG. 39****FIG. 40**

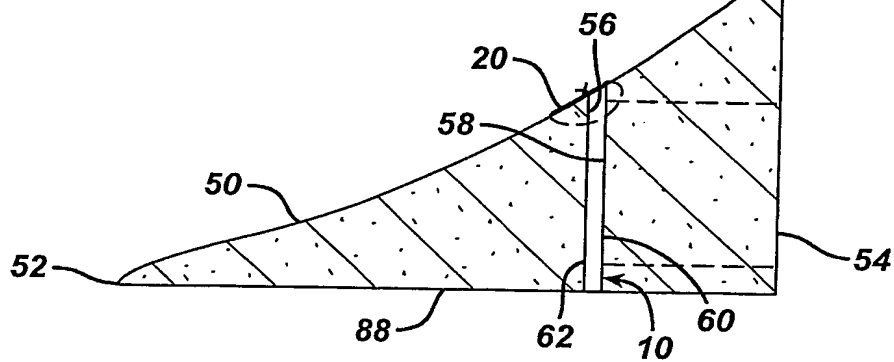
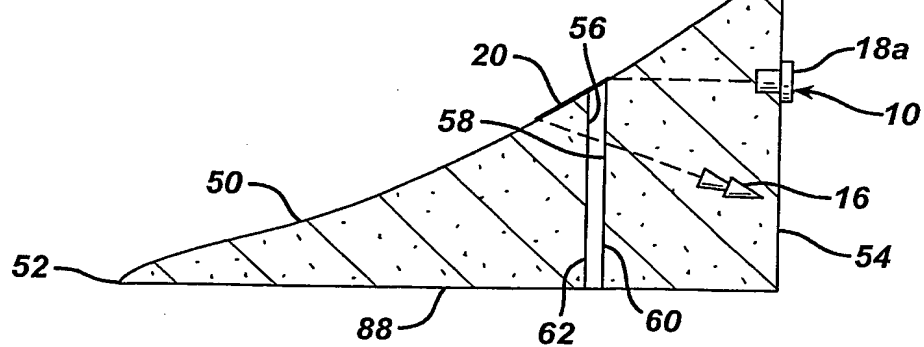
14/18

**FIG. 41****FIG. 42****FIG. 43**

15/18

**FIG. 44****FIG. 45****FIG. 46****FIG. 47**

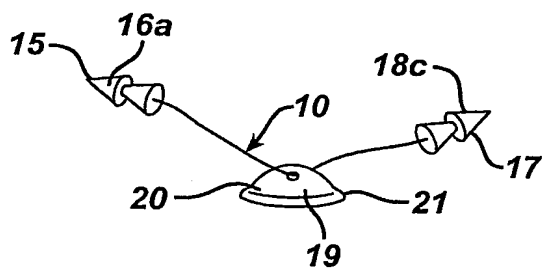
16/18

**FIG. 48****FIG. 49**

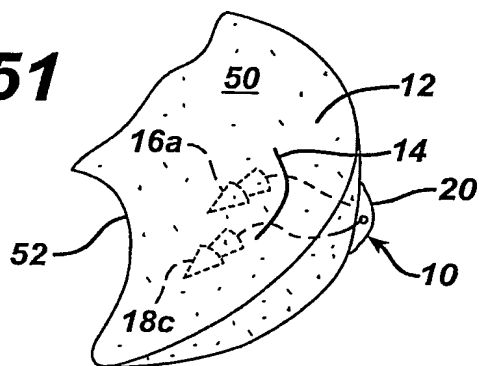


17/18

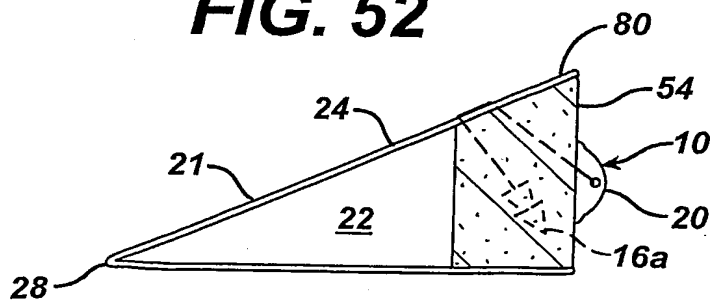
**FIG. 50**



**FIG. 51**



**FIG. 52**



18/18

**FIG. 53**

